SCIENTIFIC ADVISORY PANEL (SAP)

OPEN MEETING

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Reported by: Frances M. Freeman

C O N T E N T S

DR. ROBERTS: I would like to open this Wednesday, October 24th, meeting of the Scientific Advisory Panel.

In case there are some members of the audience who were not here yesterday, we need to go through a few administrative things to begin, and first of all, I would like to ask our designated federal official for this meeting, Ms. Olga Odiott, if she has any announcements and instructions for the panel.

MS. ODIOTT: Thank you, Dr. Roberts.

Welcome, everybody. And by way of background, the FIFRA SAP provides advice, information and recommendations to the agency on pesticides and pesticide-related issues regarding the impact of regulatory actions on health and the environment.

I would like to welcome the panel members and I would like to thank the panel members for agreeing to serve and for their time and effort in preparing for this meeting.

I also want to say thank you for the representatives from other federal agencies for their support, their involvement and the active role that they have played in preparing for today's SAP meeting.

We have a full agenda for today and tomorrow. And I just want to remind everybody that the meeting times on the agenda are approximate.

We have a significant number of public commenters and the time is very limited. So for members of the public requesting time to provide oral comments, we request that they limit their comments to five minutes as indicated in the federal register notice announcing the meeting.

Also, please direct your comments to the subject matter relevant to this meeting. This will allow adequate time for all public commenters and an opportunity for them to present to the FIFRA SAP.

We have asked the public to provide written comments of the topics or issues that are presented in advance of the meeting, and these comments have been provided to the panel for their review and their analyses.

All the background materials, all the question posed to the panel by the agency and all other document that are related to this SAP meeting are available in the OPP dockets. The overheads will be available in a few days. And the background documents are also available on the EPA web site. The agenda lists the contact information for such documents.

As a designated federal official, I work with the appropriate agency officials to ensure that all appropriate ethics regulations are satisfied. In that capacity, panel members are briefed with the provisions of the federal conflict of interest laws.

Each participant has filed a standard

government ethics report and I, along with the other deputy ethics officer for the Office of Prevention, Pesticides and Toxic Substances, and in consultation with the Office of the General Counsel have reviewed the report to ensure that all ethics requirements are met.

For press members that have questions about today's meeting, Mr. David Deegan is available to assist you. Mr. Deegan is right here. Thank you.

And like we said yesterday at the conclusion of the meeting, the panel will prepare a written report that serves basically as meeting minutes, and that report will be available in approximately 30 days. Thank you.

DR. ROBERTS: Before we get started today, we need to introduce the panel members again. So let me just ask the panel members, beginning to my immediate right with Dr. Freeman to just go around the table and

state your name, affiliation and, briefly, your expertise relative to our topic.

DR. FREEMAN: My name is Natalie Freeman. I'm at Robert Wood Johnson Medical School and the Environmental and Occupational Health Sciences Institute in Piscataway, New Jersey. And my areas of research are children's exposure to environmental contaminants and the role of activity patters as they relate to exposure.

DR. MacDONALD: I'm Peter MacDonald, professor mathematics and statistics at McMaster University in Canada. And my expertise is a general expertise in applied statistics.

DR. KOSNETT: I'm Michael Kosnett. I'm an associate clinical professor at the University of Colorado Health Sciences Center. And I'm a physician, specializing in occupational and environment toxicology.

DR. GINSBERG: Gary Ginsberg with the

Connecticut Department of Public Health. Teaching affiliations with Yale and the University of Connecticut Health Center with specialization in children's pharmacokinetics.

DR. KISSEL: I'm John Kissel. I'm in the Department of Environmental Health at the University of Washington in Seattle. And my research area is human exposure assessment.

DR. GORDON: I'm Terri Gordon, NYU.

DR. LEES: Good morning. My name is Peter Lees from Johns Hopkins University School of Public Health. I am an industrial hygienist with expertise in exposure assessment, mostly chromium exposure assessment, usually related to epidemiologic studies.

DR. HOPENHAYN-RICH: I'm Claudia Hopenhayn-Rich, an associate professor at the University of Kentucky, Department of Preventive Medicine and Environmental Health. I'm an epidemiologist and my expertise

includes a number of epidemiologic studies of arsenic exposure in drinking water.

DR. LEIDY: Good morning. I'm Ross Leidy from the Pesticide Residue Research Laboratory at North Carolina State University in Raleigh, North Carolina.

We deal with non-food source exposures following pesticide applications in and around structures and are interested in the movement of pesticides from urban and rural environments into public drinking water supplies.

DR. SOLO-GABRIELE: I'm Helena Solo-Gabriele. I'm an associate professor at the University of Miami. I'm a civil environmental engineer. And my area of expertise is in the environmental aspects or impacts of CCA-treated wood.

DR. BATES: I'm Michael Bates. I'm from the School of Public Health, University of California at Berkeley. I'm an

epidemiologist with a background in toxicology.

DR. STYBLO: I'm Miroslav Styblo. I'm a research assistant professor with the Department of Pediatrics School of Medicine and Department of Nutrition, School of Public Health at the University of North Carolina at Chapel Hill. And I am involved in the research of arsenic metabolism and the mechanism of toxic and carcinogenic effects of arsenic.

DR. STEINBERG: I'm J.J. Steinberg. I'm a professor at the Albert Einstein College of Medicine. I'm in the faculty of pathology. I work on DNA toxicology and I am involved in environmental public health.

DR. CHOU: I'm Karen Chou from Michigan State University. I'm in the Department of Animal Science, Agriculture and Natural Resources, and also with the Institute for Environmental Toxicology and the Institute

of International Health in the College of Osteopathic Medicine. I am an environmental toxicologist.

DR. MUSHAK: I'm Paul Mushak. I'm a toxicologist and health risk assessor. I direct a tox practice and I'm also a visiting professor of pediatrics at Einstein in the Bronx.

My area of expertise over the last 35 years, I guess, is exposure assessment and toxicokinetic aspects of exposures in children and young animals.

DR. FRANCOIS: My name is Rony Francois. I'm an occupational medicine physician and an assistant professor at the University of South Florida College of Public Health in Tampa, Florida. My areas include toxicology and exposure assessment.

DR. SMITH: My name is Andrew Smith. I'm and environmental health scientist and a risk assessor and director of the

environmental toxicology program within the Maine Department of Human Services Bureau of Health. And my office has had some involvement in evaluating children's exposure both to arsenic in water as well as pressure-treated wood.

DR. SHI: I'm Xianglin Shi from National Institute of Occupational Safety and Health. I'm also adjunct professor at West Virginia University.

My laboratory studies molecular mechanism of metal toxicity and carcinogenesis.

DR. MORRY: I'm David Morry. I am a toxicologist and risk assessor for the State of California, the California Environmental Protection Agency.

I did the risk assessment for chromium in drinking water for the State of California. And I am currently involved in a project to review all of our regulations to see how they

affect infants and children.

MR. CLEWELL: I'm Harvey Clewell. I just recently became a principal with Environ, but for a number of years I have been doing pharmacokinetic and dose response modeling on arsenic and chromium and, more recently, pharmacokinetics in children.

DR. WARGO: John Wargo, Yale University, professor of risk analysis and environmental policy.

DR. HEERINGA: I'm Steve Heeringa, a biostatistician with the Institute for Social Research, University of Michigan, where I direct research design and operations for that institution.

DR. MATSUMURA: I am Fumio Matsumura from the University of California at Davis. My area of interest are pesticides, biochemistry, molecular biology.

DR. THRALL: I'm Mary Anna Thrall. I'm a veterinarian and a professor of

pathology at Colorado State University.

DR. ROBERTS: I'm Steve Roberts and I'm a professor with joint appointments in the Colleges of Medicine and Veterinary Medicine at the University of Florida. I'm a toxicologist and have research interests in mechanisms of toxicity, pharmacokinetics and research risk assessment -- rather, methodology.

We have with us this morning Dr. Vanessa Vu, who is director of the Office of Science Coordination and Policy. We had a pretty full and interesting day yesterday, Dr. Vu, and I think we're probably going to have another one today. Welcome.

DR. VU: Thank you, Dr. Roberts.

Indeed, we had a very full discussion yesterday. And the agency is very appreciative of all the comments, the very insightful and thoughtful comments from panel members. We also were very appreciative that

members of the public have presented their scientific viewpoints on these issues surrounding children's risk associated with CCA-treated wood in the playground setting.

Yesterday's presentation, the agency provided you a regulatory context from Mr. Jim Jones, deputy director of Office of Pesticides Program, and our scientific staff from the antimicrobial division within EPA's Office of Pesticide Programs, as well as our colleagues from the Office of Water and region 8 scientists, surrounding both the overview of the exposure and hazard issues as well as some detailed questions on exposure.

Today we were hoping that our EPA scientists will continue to provide you some of the background on some of the exposure scenario issues which you have heard quite a bit from yesterday, discussion with all of you, and hopefully we will continue to look forward to look forward to hearing your

discussion and deliberation as we pose these specific questions in front of you this afternoon from the hazard as well as exposure for the next days. Thank you.

DR. ROBERTS: Thank you, Dr. Vu. We look forward to those presentations.

We were not able to get completely through our public comments last night, and I appreciate the indulgence of the public commenters who had to wait to present this morning, but we would like to give them the opportunity to present their comments now.

I have three public commenters listed as requesting to address the panel: Mr. John Butala, Dr. Joyce Tsuji, and Scott Conklin.

I would each of those individuals in that order to be prepared to make a presentation.

Mr. Butala, welcome. Would you introduce yourself to the panel, please.

MR. BUTALA: My name is John Butala.

I'm a toxicologist and I'm here on behalf of the American Chemistry Council Arsenicals and Wood Preservatives Task Force.

The task force would like to thank the EPA for the opportunity to present comments to the SAP. My comments will extend to about 15 minutes today, which is the amount of time I understood I was allotted. And my overheads will improve, as we go on, in legibility.

Yesterday, you heard Dr. Beck present considerations for CCA-treated wood risk that rely upon reduced bioavailability of CCA-wood surface residue, and you heard Dr. Aposhian present animal data to support that position.

You also heard Dr. Kamdem provide chemical information about the differences between arsenic and chromium in aqueous solutions and in treated wood.

The biological and the chemical work presented by these scientists is meaningful to the risk assessment, and my purpose today is

to focus attention on an important data set developed on CCA-treated wood in relevant mammalian species that demonstrates the manifestations of the physical and the chemical aspects of CCA-treated wood, aspects which you have been hearing about for the last several days from Drs. Kamdem and Aposhian.

To equate risks from CCA-treated wood with inorganic arsenic is inappropriate. The form in which arsenic exists, the form to which exposures occur influences physical chemical properties, such as water solubility and biological properties such as toxicity. The trivalent form of arsenic in general is taken to be more toxic than the pentavalent, inorganic form, and these inorganic forms are taken generally to be more toxic than the organic arsenicals, although we now know there is evidence that the valent state of arsenic in the methylated derivatives may be a major factor in toxicity.

We also know that the majority of the acute toxicity data historically supports the statement as I have read it to you, and that it is in vitro data that support at moment indications that methylated metabolites have increased toxicity than heretofore expected.

We know that there is 3000fold difference in mouse acute oral toxicity between arsenic trioxide and arsine. In fact, the most toxic form of arsenic is a gas, arsine.

These differences have relevance to the toxicity of arsenically treated wood. When wood is pressure treated with CCA, chemical reactions occur between the components of the CCA preservative and the wood.

The results are the reactions are changes in the valence state of chromium and the solubility of chromium, arsenic and copper from CCA to yield stable complexes of the

metals with wood carboxylates, predominantly in the wood cell wall. The overall reaction process is termed fixation and is the process that renders the CCA components strongly fixed to the wood, thereby conferring the preservative property of the wood. The mechanism of these reactions has been the subject of much research, recently summarized by D.C. Bull, and we heard a little bit about that yesterday.

And just to capture that, at least of one of Bull's publications, the work presented, as well as that of Kamdem yesterday that we heard, demonstrates that once fixed with wood cellulose, the chromium, the copper and the arsenic metals of CCA exist predominantly as water-insoluble complexes with other organic and inorganic components. This was specifically demonstrated for CCA-wood surfaces by Kamdem in the x-ray diffraction work that he presented, indicating

that CCA solution is different from samples of the surface of treated wood as opposed to CCA fixed on treated wood, and that CCA-treated and untreated wood surfaces subjected to scanning electron microscopy showed that solids present on the wood surface were amorphous complexes of oxygen, of carbon, of calcium, chromium, copper and arsenic and iron, and that the deposits on the CCA-treated wood surface, once fixed, were amalgamation complexes of those elements and that the solid deposits did not contain arsenic pentoxide or trioxide.

Finally, we know that the surface residue on CCA-treated wood contains less than half of a percent copper, arsenic or chromium. And of that half a percent, only about 10 percent of the arsenic on the surface of the treated wood is water-soluble. That computes to about .05 percent of the residue on the surface of treated wood to be water-soluble

arsenic.

It is inappropriate, as I indicate up there, to equate risk from CCA-treated wood with water-soluble hexavalent chromium, just as it is inappropriate to equate it with arsenate. The water-soluble hexavalent chromium I'm speaking of, of course, is equivalent to the test material that Dr. Tyl used in her developmental toxicity studies in rabbits and in mice. These would be the studies that EPA has identified for hazard assessment -- short-term hazard assessment of chromium.

As stated above, when wood is treated with CCA, a number of chemical reactions occur, one of which is the change of hexavalent chromium to trivalent chromium, reduction. The reactions begin as soon as wood is treated with CCA and continue until essentially all of the chromium is fixed. McNamara showed that fixation is time,

temperature, and moisture-dependent. In his work on fixation, McNamara equated fixation with a conversion of hexavalent chromium to trivalent chromium and used squeezed solution of CCA-treated wood as the medium to measure the fixation.

In these studies -- and I do believe copies of all of the studies that I'm referencing and that I will reference have been given to this panel; you should have those, as well as the full bibliographic citations for the studies I'm referencing, and copies of the comments.

In McNamara's work, the term "completely fixed" corresponded to greater than 98 percent fixation, and also a negative chromotropic acid fixation test result.

This early work comports very well with what we heard yesterday from Dr. Kamdem, that 98 to 99 percent of the chromium in CCA-treated wood is reduced to trivalent

chromium. Accordingly, the Tyl study that I mentioned a few moments ago is inappropriate for risk assessment on CCA-treated wood in that essentially no water-soluble hexavalent chromate, or very little water-soluble hexavalent chromate is present in treated wood.

A limited but important body of toxicology data demonstrate that the chemical form of arsenic as it exists in treated wood -- and I'm speaking of sawdust now -- and on treated wood surface as the dislodgeable residue is not equivalent to soluble arsenate and arsenite. And when I say limited, the limitations I'm referring to concern the number of animals in the study. The study designs were solid, the analytical chemistry was solid, and I think the toxicology was solid, but clearly the number of animals is small.

Because of this, the chemical and

physical properties, the toxicological properties of the arsenical compounds from CCA-treated wood are different and distinct from soluble arsenic species in water. A demonstration of this can be found in the tox studies I'm referring to. The first of these were done by Drs. Peeples and Parker, working with beagle dogs.

Peeples and Parker fed the animals CCA-treated wood dust using southern pine treated wood. The dogs' daily dose of wood dust was approximately .15 grams per kilogram for 13-kilogram dog. Peeples and Parker measured the amount of arsenic the dogs consumed on a daily basis as 6,000 micrograms per day from treated wood, and an additional 135 micrograms per day from the standard lab trial. So they were getting about 6.1 milligrams of arsenic per day.

Feedings continued for eight consecutive days, for a total wood dust dose

of 1.2 grams per kilogram, equating to about 49 milligrams of arsenic as the element.

This dosing scheme equates to approximately 0.47 milligrams per kilogram arsenic -- 0.47 milligrams of arsenic per kilogram per day or about 3.8 milligrams per kilogram arsenic, total dose over the course of the study. There were no adverse clinical signs noted in the eight-day dosing period. Urine analysis, germ analysis, hematology values were unchanged as a result of dosing.

About 60 percent of the ingested arsenic was found in the feces and 40 percent of the ingested arsenic was excreted in the urine, suggesting that the bioavailability of arsenic from CCA-treated wood ingestion was about 40 percent.

The majority of the urine arsenic was dimethyl arsenic. No trimethyl arsenic was detected. Again, this comports with what we heard yesterday, albeit in a different

species.

Peeples also conducted a higher-dose study in which he fed dogs ten grams of CCA-treated wood dust daily for five days, to yield a daily dose of 39 milligrams of arsenic, or about 3 milligrams per kilogram per day as the element.

The dogs demonstrated no signs of toxicity during treatment. Fecal excretion varied from day to day, ranging from 23 to 100 percent. The average amount of dosed arsenic excreted in feces during dosing was approximately 74 percent. The average amount of arsenic excreted in urine was 16-1/2 percent, again, indicating a low bioavailability of arsenic from ingesting treated wood.

In this study, however, done in higher doses, pentavalent arsenic was found in the urine, along with dimethyl arsenic.

Now, this table helps, I think, to put

the studies that I've just talked about into perspective. And what I'm getting at here is Peeples fed dogs CCA-treated wood sawdust that contained amounts of arsenic which, if given in pure form, would likely to be lethal to the dogs and, for that matter, to humans. The health of the dogs, however, was unaffected, and all of the arsenic was excreted in feces or urine, essentially all. This was possible because the forms of arsenic in the wood was not soluble inorganic arsenic, thus reducing the bioavailability of arsenic in the wood dust.

Now, the utility of this study is not to present an argument for which species is an appropriate species to assess arsenic or CCA-treated wood toxicity. The utility of this particular table is to look at the intra-species differences between arsenic pentoxide toxicity and CCA-treated wood within a species.

Dr. Peeples also investigated the potential for trans-dermal absorption of arsenic from CCA-treated wood dust in contact with skin. In this study, beagle dogs had 1.5 grams of wood dust, which is about 45 milligrams of arsenic, applied under a patch to clipped skin, applied continuously for two days. Peeples was able to detect background levels of dimethyl arsenic in the urine prior to wood dust application -- that would be dietary arsenic -- and found no increase in urinary excretion of inorganic arsenic during the application period or for two days after the application period.

The University of Alabama study, which used pregnant rabbits exposed dermally to CCA sawdust for days 7 to 20 of pregnancy similarly provided no evidence of any treatment-related effect in the rabbits. The pregnant animals received 26 grams of CCA-treated wood dust on days 7, 11 and 15

through gestation. The test material remained on the skin under vinyl plastic film until gestation day 20.

Maternal response to dermal dosing stress was equivalent in treated and control groups. According to the author of the study, there were no differences between the treated and control groups in gross, skeletal or visceral malformations, indicating that extended dermal exposure to CCA-treated wood dust is not teratogenic or phytotoxic.

Hood also tested pregnant mice with dietary exposure to 10 percent CCA-treated wood dust and untreated wood dust and a second control group was employed that received lab trial and no wood dust.

Maternal arsenic exposure via dietary admixture of CCA wood dust throughout pregnancy, gestation 1 to 18 days, produced no effect on maternal weight gain, no effect on fetal parameters, including fetal toxicity,

and no skeletal or visceral malformations when compared to untreated wood dust control or to no wood dust control.

In vivo cytogenetic studies have been completed in mice receiving dietary exposure to CCA wood dust for up to 21 consecutive days. 50 metaphase plates at a minimum of a thousand mitotic figures, were scored for each animal. No changes were observed in chromosome number or structure. And in the same study, blood cell parameters, which were via red cell count, white cell count and differential as well as hemoglobin and hematocrit, were examined and found to be unaffected by 21 days of oral dosing by gavage of 2500 milligrams per kilogram per day. And I think this table summarizes those.

Incidentally, the asterisk, if you can see it, indicates my assumptions on calculating the dose levels from dietary admixture which I can explain later, if you

like.

In a study to be published in an upcoming edition of Toxicological Sciences, Gordon, et al. -- and that would be one of your panel members here, Dr. Terri Gordon -- showed that in vitro exposure of V79 hamster, Chinese hamster, along fiberglass cells to respirable-size particles of CCA-treated wood dust produced greater cytotoxicity than equivalent exposure to untreated wood dust. Gordon also showed that increased cytotoxicity with CCA wood dust occurred in an arsenic-resistant cell line, suggesting that arsenic was not responsible for the cytotoxicity.

Tagacytosis (ph) of the particles appeared to be necessary to induce cytotoxicity.

Metalothioneine (ph) induction due to copper was the only effect reported as a result of cell exposure to particle-free

extracts of the treated wood.

Aged samples from treated wood were less potent than fresh samples. At approximately equal molar concentrations, the cytotoxicity of the treated wood was less than 30 percent of the cytotoxicity of the inorganic arsenate or hexavalent chromate when tested as the aqueous solutions.

As illustrated by this collection of studies presented here and when matched by test animal species and endpoint, it's possible to observe a marked reduction in general toxicity and specific toxicological endpoints for CCA-treated wood versus inorganic arsenic and chromium. This is possible because the metals in CCA-treated wood are not equivalent to inorganic water-soluble arsenic and chromate and because the bioavailability of these metals in CCA-treated wood is reduced.

So in summary, the evaluation of

CCA-treated wood in a manner that is more relevant to the physical chemical and toxicological properties of CCA-treated wood must be part of considerations by the SAP.

The interpretation of exposure data for CCA-treated wood has been and continues to be based on inorganic arsenic toxicity information, which, in turn, these informations are based on controversial low dose extrapolations of cancer and non-cancer endpoints from high-exposure inorganic arsenic drinking water studies. And this is inappropriate for hazard assessment and risk assessment for CCA-treated wood.

The oral bioavailability of arsenic from treated wood particles is far less than 100 percent. I think we now have several demonstrations of that. And a proper risk assessment for CCA-treated wood must integrate exposure assessment, bioavailability and toxicology data derived from studies of

treated wood.

Those are my comments. Thank you very much for your attention.

DR. ROBERTS: Thank you, Dr. Butala. We have a number of questions for you.

Dr. Mushak and then Dr. Shi.

DR. MUSHAK: Two quick questions and a cautionary comment.

The first question: The aging factor in dusts. Did Peeples' study use freshly-generated dust?

MR. BUTALA: The Peeples' study did use freshly-generated dust.

DR. MUSHAK: And they did not, as I recall, look at the effect of aging of dust on release. So I think we have to be careful about --

MR. BUTALA: You are right. They did not.

DR. MUSHAK: The second one is, since we don't know exactly what's in the medium

that Professor Aposhian used for his hamster studies, I think -- are you comfortable assuming that, since apparently you are big on form of arsenic and form of chromium, that we have to be careful about the form going into the hamsters?

MR. BUTALA: I am big on the forms of the metals.

DR. MUSHAK: Okay. Right. But consistency --

MR. BUTALA: Now, as far as what Dr. Aposhian has done, based on his presentation yesterday, which was my first chance to see the data and hear his explanation, no, we don't know the form.

But I understand, and it's my understanding we probably need to verify this -- I understand that Dr. Kamdem's lab, who prepared that extract -- I believe that's the case -- also has retained samples and either has done or is doing analytical

chemistry assessments of the solutions that were used for dosing.

So it's my expectation that we will get some analytical chemistry insight into what the animals received.

DR. MUSHAK: That would be chemical structural, not just simply bulk analysis, right?

MR. BUTALA: Well, that's my impression, yes.

DR. MUSHAK: The comment goes to the issue of trivalent versus pentavalent arsenic differential toxicity. I mean, that's from the old literature of acute high dosings in mice and rabbits, et cetera.

I think, with the range of exposures we're talking about with these kids -- and Dr. Aposhian essentially verified this yesterday -- one ought not to belabor this trivalent-pentavalent differential toxicity business. It's a bit misleading.

DR. ROBERTS: Dr. Shi?

DR. SHI: I have several questions or comments -- or clarification, actually. The first one is you stated that when the wood are treated and the chemical reaction occurred -- which kind of chemical reaction are you talking about here?

MR. BUTALA: These reactions are -- there are a series of reactions, and collectively they are called fixation, and I think that one of the final public commenters today will address that at some level.

The fixation reactions have been the subject of a lot of study. And, again, I think we heard that yesterday. I'm talking about the chemistry of it now. And there have been reviews published on those. Probably the most recent review and perhaps the most insightful is the one cited in my presentation by D.C. Bull and others.

And I can't really provide you with a

thorough description of it at this point except to say that, in essence, the important aspects of fixation are that the CCA-treating solution, the registered pesticide, is an aqueous solution of arsenic acid, chromic acid and copper oxide. And the acid forms are the oxide. So it's arsenic pentoxide, chromic oxide and copper oxide. Pentavalent arsenic, hexavalent water-soluble chromium and copper oxide.

When in contact with the wood, the first thing that seems to happen are oxidation reduction reactions with the chromium that change the valent state from hexavalent to trivalent, which then cause subsequent reactions which change the water solubility of the arsenic and the copper through the bonding of, I think, the sugar moieties in the cellulose wall of the wood cells in the wood.

Now, that's not a very sophisticated chemical explanation of fixation, but that's

essentially what occurs such that, in the end, when fixation is complete, the chromium has undergone a valent state change. The other elements do not undergo a valent state change, but all three elements undergo solubility changes. And that then confers -- well, the term "fixation" then relates back to that end product which then confers preservative characteristics to the wood itself.

Fixation is typically measured by the amount of chromium that remains in the hexavalent state. Any amount that remains in hexavalent state is an indication of the absence of fixation.

DR. SHI: How about arsenate? You talk about the chromium -- from Chromium 6 to Chromium 3 meaning completion of a fixation. How about arsenate?

MR. BUTALA: Again, we may hear about this a little later, but chromium is essentially the rate-limiting component of the

fixation reactions.

So that -- I'm sorry. It's not the rate-limiting components. The other two are. Probably, arsenic is. So that arsenic undergoes the solubility change and copper undergoes the solubility change as chromium is being reduced.

And those changes occur either simultaneously and those reactions occur -- are finished prior to the complete reduction of chromium.

So that chromium is what is measured as the endpoint of fixation. And it's the reduction of chromium from hexavalent to trivalent.

DR. SHI: Second question. You said -- you identified some compound. Because your presentation contained a lot of information, I don't exactly understand what's the compound you identified.

Did you use that compound exactly the

same -- use that to evaluate the toxicity or carcinogenesis?

MR. BUTALA: The compounds I identified, that reference came from the work of Dr. Kamdem that was presented yesterday. And that was analyses that he performed by several methods, several physical methods on the residue of CCA-treated wood.

The toxicological data that I presented was done on sawdust, you know, ground-up wood.

There was no attempt made in the preparation of the sawdust to remove surface residue, so that was present as well.

Now, if you are asking me was the type of analysis that Dr. Kamdem performed to identify these inorganic arsenic and organic complexes, was that kind of analyses performed on the dosing -- on the material that was dosed to the dogs and to the rabbits in the studies I described? The answer is no. The

analyses done there were just elemental analysis by atomic absorption.

DR. SHI: Another question. This is Number three.

The experiments are performed in the laboratory, as actually most experiments do.

And recently there are several studies, and one is from NYU. And Dr. Terri Gordon is also familiar with that.

Another study is from the University of Minnesota.

In the last two or three years, the studies show, when you do the toxicity carcinogenicity study in the laboratory, it may be very different than in a field study because of UV of the sunlight, particularly in a playground. Children play in the sunlight. The sunlight or UV enhances the arsenic toxicity and carcinogenicities.

Do you have any comment about that? Do you consider that factor in your toxicity

study?

MR. BUTALA: The comment I have -- I'm not familiar with Minnesota work, but I am familiar slightly with work that Toby Rossman has done at New York University where she first demonstrated that inorganic arsenic, anyways, could be co-mutagenic or at least co-genotoxic in the presence of ultraviolet radiation. And I think the end point of her genetic toxicity was chromosome damage as opposed to point mutation. Again, I did present some data here that indicated that CCA-treated wood sawdust did not cause any sort of chromosome damage in vivo.

Then I think Dr. Rossman extended those studies very recently in a publication where she indicated that inorganic arsenic can be a cocarcinogen in a mouse model in the presence of UV light, and I think that's what you are referring to.

So those endpoints, genotoxicity,

specifically chromosome damage, and carcinogenicity, are the two endpoints that have been associated with ultraviolet light co-activation, for lack of a better term.

We have evaluated one of those here, the classgenicity (ph). I'm not aware of anybody -- of any work that has been done on carcinogenicity in an animal model, particularly the one that Dr. Rossman has developed, that uses sunlight exposure as well.

DR. SHI: And everybody talks about in the treated wood about arsenic and chromium together. And you also talk about a possible interaction. And most likely, they can form a cluster of some kind of compound together. The two questions -- two points here.

One is in the arsenic and chromium compound, if together, that's a new compound. It's one. Secondly, the synergistic effect. Did you consider these two factors? One is

the compound together, the new compound. Second, is the synergistic effect about the two compounds.

MR. BUTALA: The first part of your question as far as considering that complex, it's my position that the complex was present in the material dose to the rodents. So I think it's fair to say, yes, it was considered in the toxicology evaluation.

The second part of your question, were you asking about synergistic effects?

DR. SHI: Yes.

MR. BUTALA: Well, again, my answer would be the same in that the material of concern, in this case the complex, and certainly the complex representing all three of the elements in whatever form, was the material tested. That was really the point I was trying to make, that the relevant test material for evaluation of CCA-treated wood hazard should be CCA-treated wood, as opposed

to this one step beyond extrapolation of what is known about arsenate or arsenite, what is known about chromate, chromium. And then trying to synthesize those together and then having to deal with the uncertainties of interactions and different test systems.

It seems to me if you want to know about the hazard of CCA-treated wood, that's what you should test.

And that's what I described.

DR. SHI: Last question. For the cigarette smoking, for example. That took about 10 years or 20 years for the cancer to develop, and the cancer take a long time. How about CCA-treated wood? How long do you study and how long do we need it to getting your conclusion? It's not that bad. How about the long-term effect to make --

MR. BUTALA: We do not have long-term toxicology studies on CCA-treated wood. You are correct.

DR. SHI: In your study, how long your study will evaluate? You have some evidence to show another toxic -- what's the time frame of that study?

MR. BUTALA: The time frame of the study? The longest dosing period was 21 or 22 days. So you are correct. These are -- these can be characterized as single dose or, at best, repeated dose studies. That's what I presented.

DR. ROBERTS: Dr. Ginsberg.

DR. GINSBERG: I wasn't aware -- well, I was aware of the Peeples study. I hadn't read it, though, so I appreciate you bringing that to our attention. I would just like to understand it a little bit better.

You said that under one dosing scenario, there was something on the order of 40 percent excretion in urine. So at least, as a minimum, 40 percent bioavailability of the arsenic that was in the wood dust. And

then, with a higher dose gavaged of the wood dust, there was 16 -- so a minimum of 16 percent bioavailability.

So I would like your comments on two things. One is, how much of the material -- what was the difference in dose between the 40 percent minimum bioavailability study versus the 16 percent? What were those amounts of wood dust going down the hatch, so to speak?

And then the other is your opinion, I guess, on if that was dislodgeable residue rather than wood -- actual bulk wood dust going down, do you think that we would have seen more bioavailability in that study.

MR. BUTALA: The difference between the two -- you are right. I mean, you have put your finger right on it. Both were -- no, I'm sorry. I think it would be more -- the first study was, in fact, a dietary study so it was a dietary admixture. And the second study, I think, was more of a bolus dose to

get -the ten equivalent of 10 grams of wood per kilogram down into the animal.

I think that alone could explain the differences in bioavailability and absorption, really. So that's the first part.

And the second part you asked me?

DR. GINSBERG: In your opinion, do you think that the -- if the way the material was dosed was as dislodgeable residue rather than the arsenic contained in bulk wood dust, would there have been any difference in the amount we would have seen in urine?

MR. BUTALA: That's very difficult to say. When Peoples did his work, there was not attention focused on surface dislodgeable residue.

Now, there was nothing special done to the wood that would have removed the dislodgeable residue, particularly the type of treatments of the wood that we heard and saw described yesterday.

The really -- the big difference, I think, that has to be accounted for is the increase in surface area of the treated wood when it's made into sawdust. A tremendous increase on a weight basis of the surface -- the particles that I think probably adds an element of conservatism to toxicology hazard assessment of CCA-treated wood on the one hand because, on a weight basis, the increase in surface area of the particles versus not increase in surface --

DR. GINSBERG: But when comparing that to the dislodgeable residue that we don't have that extraction step, aren't we dealing with different matrix for bioavailability? I know the arguments you are describing in terms of the complexation and that the arsenic may be in a form that's not sodium arsenate in terms of bioavailability. That's a separate issue. But when we're talking about what's in wood -- I know it's not solid; it's ground-up wood

dust compared to dislodgeable.

I just wanted to see, in your mind, if you thought they were equivalent bioavailability or do we know what the difference in -- has anybody done that bioavailability test dislodgeable residue versus ground-up wood?

MR. BUTALA: They are not equivalent. They cannot be equivalent. All I'm prepared to say is that the wood dust that was administered to the animals had whatever surface residue is typically present on that wood still on it as wood dust and the animals received it. The endpoints of the study, which would be the reduced toxicity, systemic toxicity, which was measured, and the apparent reduced bioavailability -- blood levels weren't taken in these studies, but excreta were measured for the elements, so there is pretty good evidence for reduced bioavailability.

Some component of that was the reside, and that's as far as I'm willing to --

DR. GINSBERG: And one final question. Do you know what the pH of the dog's stomach is?

MR. BUTALA: No, I don't.

DR. GINSBERG: It is pretty acidic.

MR. BUTALA: But just to circle back to that, remember what I said. I did not present any of these data as an argument for appropriate species for toxicology hazard assessment to people. It's not an inter-species exercise that I was going through. It's an intra-species. It's dog arsenate versus dog CCA-treated wood. So whatever the pH of their stomach was, it's not important to me because I'm not trying to say that the dog was a surrogate for a human. I'm just saying that than animal model behaved differently in terms of how it responded to aqueous arsenate versus CCA-treated wood.

DR. ROBERTS: Dr. Clewell and then Dr. Styblo, Steinberg and Mushak.

DR. CLEWELL: My question has already been answered. Thanks.

DR. ROBERTS: Dr. Styblo?

DR. STYBLO. I have one or two short comments.

We repeatedly discussed the question of bioavailability here based, basically, on comparison of urinary excretion and total, urinary plus fetal excretion. Remember, we are talking arsenic here.

We have clear data from experiments in animals that say that arsenic is excreted in bile, not just inorganic arsenic, but also metabolites of arsenic.

Considering this fact, I'm not sure it's a good idea to use this ordinary formula urinary compared with total excretion for assessment of bioavailability. In fact, what is in bile are most toxic arsenic metabolites,

including carconite in complex with glutathione, and MA3, which is the most toxic one, in complex with glutathione.

There is evidence for that. So for me, the fact that significant part of arsenic is excreted in feces doesn't mean that this arsenic has not been absorbed in intestine.

To make it even more complicated, we know that intestinal microflora can methylate arsenic to forms that may be reabsorbed in the organism. So this is a very complicated issue and there is great level of uncertainty.

Second thing. You seem to downplay a little bit cytotoxicity studies done with methylated arsenicals compared with in vivo studies. I would like to clarify this thing.

You are right. Methylated arsenicals in trivalent forms were tested mainly in cultured cells as compared with other previous studies done in animals. I would like to balance the advantages and limitations here.

The cells were, in part, primary human cell lines, primary human cell lines derived from target tissues and tissues that methylate arsenic: Liver, skin, bladder and bronchs (ph), which seems to be very relevant material. So that's the advantage.

The limitation is the fact that we are working not in vitro, but ex-vivo conditions, which are not completely comparable with in vivo.

While in animal studies, we are working with animals in vivo. However, we know that we don't have at this time a good animal model for either human methylation or metabolism or toxic effects of arsenic.

So that would be a balanced view of the toxicology of arsenic.

MR. BUTALA: And I appreciate the balance. I'm just pointing out that, you know, at the level of the in vitro studies, we lack the pharmacokinetic component of the

in vivo study, which I'm sure will come.

DR. ROBERTS: Dr. Steinberg. Then Dr. Mushak.

DR. STEINBERG: Mr. Butala, the amiable presentation of Dr. Aposhian really was a pilot study. It was five animals. There was no genetic information. It would -- it was not a peer-review article. It clearly did not make a scientific standard as opposed to just a little brief bite of information. So it's hard to use that information in any decision, and I think we can all pretty much agree to that.

Regarding Dr. Kamdem, again, in a non peer-review paper that we received, his little report that we received, the x-ray diffraction is, by his own admission, semi-quantitative, which he fully admitted to, and, of course, had never been correlated with the gold standard of atomic absorption or anything else.

So, again, that really doesn't quite make the scientific standard that anyone can really use for any type of information.

Regarding your genetic toxicology, you didn't notice, or maybe you didn't mention that there were micro-nuclear damage that was caused by arsenic. And, of course, many of those studies are now -- this is a rapidly changing field. They are now old studies. Dr. Abernathy, who has worked on this, has presented the newer data of Mesa, which looks like arsenic as a very good -- a very good, directly toxic agent on DNA, which, of course, would strongly support its carcinogenicity, which, of course, the EPA, the NAS, the ATSDR and everyone agrees upon.

The Peeples data without a reference, and much of the other data that you give us is hard really to comment. We haven't received any of that data.

So -- and, also, in the Beck report,

in both her introduction on page 3 and on page 55, there was even a question raised about whether arsenic was carcinogenic, which I was a little concerned about.

So much of that information that you bring forward is very hard to use, based on it's either early form -- and, therefore, to use the term "inappropriate," I would deem is a little harsh.

MR. BUTALA: Well, I think Dr. Aposhian has indicated he is extending his work and, yes, this is an early phase. He wanted to be able to present -- to give this panel the benefit of what he was doing and where he was going.

With regard to Dr. Kamdem's work, I think he does have plans to present it to a journal, but, again, wanted to give the panel the benefit of information. And we may need to get clarification on a point, but I thought yesterday he said that he did tie his work

back into a qualified standard -- to a certified standard through atomic absorption or other means.

DR. STEINBERG: Not in the report -- and, again, I underscore report -- on his own stationery which did not appear in a peer-reviewed paper and, again, underscored a semi-quantifiable, which means not completely quantifiable. It means not linear. That's what semi-quantifiable means.

MR. BUTALA: And as to the rest of the work that I presented, I think I did provide this group copies of all of those papers. It's my understanding you have them, so you can look at them.

DR. STEINBERG: If I have them, I read them. So someone will have to show me those papers in detail because there ain't nothing that I received that I didn't read. So I will have to take a look at many of those references from '79 and, you know, those kind

of older references in genetic toxicology.

I look forward to seeing that historical, ancient data. And, again, I'm much more interested in something a little more recent.

DR. ROBERTS: Let's take a couple more questions quickly. And we can move --

MR. BUTALA: And just finally, to respond to the last point, yes, I am aware of more recent data that indicates that arsenic -- again, in the inorganic form, can be shown to interact with genetic material.

The point I was making is not to deny that in any way, but to say that when present in the wood, dose that -- essentially heroic doses, we didn't see that. That's the key.

DR. ROBERTS: Questions from Dr. Mushak and Dr. Gordon, and then let's --

DR. MUSHAK: Quick questions.

The reason I brought up this whole business of new dust versus aging dust is

really focused on the potential for generating over time more dislodgeable residues as these dusts age.

Now, would you agree that, as these dusts age, they are apt to reduce more material rather than keep them intact?

MR. BUTALA: I couldn't comment on that. My only experiences with new dust and aged dust have to do with chemical changes on just elemental aspects of the dust, lead, zinc, you know, those kinds of fumes that age, and we know there are toxicological differences there.

But whether or not those translate to structural differences on these complexes, I don't know.

DR. MUSHAK: So in point of fact, one can't rule out that aged dust would have dislodgeable residues.

The business of bolus feeding versus how children ingest materials in the course of

a day, the Peeples study with the 16 percent is a problem because it's a bolus dose, and we know that anytime you look at bolus dosing -- this is Mike Ruby's study with rabbits; it's also the studies with -- Jerry Freeman's studies with rats -- you find that these don't simulate real-life conditions for children.

And there is a big difference in the biochemical and biophysical milieux of the stomach when you whack the gut with a big dose of something and competes with the biochemical apparatus versus how a child can, you know, keep this thing going.

So you agree that the bolus artifact may, in fact, impair a direct translation to, say, child uptake rates?

MR. BUTALA: No. I agree with you. I think that the dietary studies are the better of the two. And I would also point out that the Tyl study on hexavalent chromium was a bolus dose study.

DR. ROBERTS: Dr. Gordon?

DR. GORDON: In the Peeples study, you said they did a dermal absorption with the sawdust?

MR. BUTALA: Yes.

DR. GORDON: And there was very little arsenic absorbed, right?

MR. BUTALA: Yes, very little.

DR. GORDON: But then in the physical form, wood dust -- having worked with it, it's dry, has to be compressed -- do you think there would be a difference in absorption between wood dust put back on the animal versus soil on the hands of a child or an adult?

MR. BUTALA: I think -- you know, the difference may well be not only in the matrix but in the degree of hydration. And these were not occluded dermal applications; they were only semi-occluded, meaning gauze, so there wasn't really a high level of hydration.

And I think that would be probably be a bigger factor than the medium.

DR. ROBERTS: Thank you, Dr. Butala, for your comments -- I'm sorry.

Dr. Matsumura?

DR. MATSUMURA: I'm interested in your statement that the CCA appears to be less toxic than the arsenic, arsenate, arsenite in the same species, right?

Now, when you are giving those doses, when you say 150 milligrams of the dust, you are not expressing that in the form of arsenate or arsenite. You are comparing total weight of dust versus the inorganic arsenic?

MR. BUTALA: In the actual -- in the actual study reports, in some instances, the investigator does not express dose beyond the amount of wood dust given in a standard dosing metric, milligrams or grams per kilogram.

What I did in my presentation, which, again, I believe that copies have been

distributed to you all, written copies, but if not, we can certainly take care of that -- I did those calculations you talked about. I think that's why maybe the presentation was a little bit dense because I did try to express wood as a function of dose and then the element as a function of dose.

So that's how did it and that's how I constructed the tables.

DR. MATSUMURA: So you compared milligrams to milligrams of the arsenic equivalent in the same species to make that conclusion or not?

MR. BUTALA: Yes. I did that.

DR. MATSUMURA: I would like to look at that. So I can look at my own calculation to see how equivalent they are.

MR. BUTALA: Of course.

DR. ROBERTS: Thank you.

Dr. Smith, a quick one.

DR. SMITH: Thank you for your

indulgence.

I only have the abstract for the Peeples study, but I'm curious. They sort of discuss in one of the studies they are giving ten gram of this 60-mesh sawdust. And they talk about the arsenic content of it, so I can imagine how you might get your estimate of arsenic dose.

They also say, though, that the arsenic was fully extractable in one normal HCL. Can you talk to me a little bit more about what they actually did there. I assume this is before giving the animal -- they did some sort of experiment --

MR. BUTALA: This is a separate study.

DR. SMITH: A separate study. Are you familiar with --

MR. BUTALA: A separate demonstration on their part where they took the sawdust -- you know, the idea is that, is fixation reversible under acidic conditions, low pH

conditions? And they took some of the sawdust and simply put it in HCL and found that, indeed, at -- I believe it was -- was it one normal that he used?

DR. SMITH: I think that's what --

MR. BUTALA: At one normal HCL, indeed, the fixation reactions could be fairly well reversed and free metal released.

So that then really added impetus, given what we know about the pH of the stomach, to look into whether or not that occurs in vivo.

And for reasons that have yet to be elucidated, it does not occur in vivo, at least the way it did in the HCL study.

And there is really no additional information, I believe, beyond what I've just provided to you in the actual reports.

DR. ROBERTS: Thank you, Mr. Butala. I appreciate your presentation and answering our many questions.

MR. BUTALA: And thank you for the opportunity.

DR. ROBERTS: Our next public commenter is Dr. Joyce Tsuji from Exponent.

Welcome. And could you please introduce yourself for the panel, please.

DR. TSUJI: Thank you. I'm Joyce Tsuji. I'm a toxicologist with Exponent. And I was asked to review EPA's evaluation by the American Forest and Paper Association.

Today, I'm just going to talk about two issues in the interest of time: The short-term arsenic toxicity value or values, and then dermal uptake. I'm just going to say some general things about dermal.

Regarding the arsenic short-term toxicity value, it's the same for short-term or intermediate-term. And this is the way that EPA defines, 1 to 30 days or 1 to 6 months.

They selected a lowest observed effect

level of .05 milligram per kilogram per day based on the Mizuta study. And, as you know, the margin of exposure is 100, which is made of two factors of ten, one to convert maybe the LOAEL to the NOAEL, or to take into account the inter-species sensitivity, and another factor of ten for the severity of effects. And EPA is requesting comment on what they did here.

So what this means is -- you know, this is your standard dose response curve in toxicology, dose on the X axis. The lowest effect level is at some level. Below that is a no-observable effect level.

Then you incorporate a margin of exposure. And as I understand, below that margin -- at the bottom end of that margin exposure below the NOAEL or wherever they think that is below the LOAEL, there is this threshold for concern. And that's where I guess EPA would become concerned about CCA or

arsenic exposure from CCA.

The next slide is my comment on that. When we looked at the general arsenic literature, however, there seems to be kind of a disconnect between what is being called -- what would be a threshold concern for short-term exposures versus what we know from longer-term exposures, for example, subchronic -- the subchronic literature. Part of that might be due to the very high uncertainty in the Mizuta, et al., study. I'll explain a little bit more about why that LOAEL may be underestimated compared to the severity of effects observed, and also the margin exposure appears to be quite large.

Next slide. This is kind of the order of dose response assessments we -- or curves that we would expect from basic toxicological principles for different periods of exposure. The chronic dose causing effects is much lower usually than the acute or subchronic or

subacute.

And this is true even though the effects may be different. In the short term you would expect more direct -- for example, gastrointestinal irritation caused by arsenic, whereas for the chronic effects, they are going to be more cumulative in nature.

Next slide. So the expected order is, to recap, acute, short-term, or subchronic, chronic. But when we look at the available toxicity values from the various agencies, we see a different order, and it's out of order. It's subchronic, acute, short-term -- and short-term is very similar to the chronic value, actually, for arsenic.

Next slide. And to just lay them up so you can see these values, here is the short-term RFD from region 8 that was reviewed by Oswer. And that's .015. The ATSDR or provisional acute MRL is .005. And the EPA proposed -- by EPA OPPT -- OPP has proposed a

short-term LOAEL. When you consider the margin of exposure, your dose is lower than the chronic NOAEL and pretty similar to the chronic RFD. So there seems to be sort of a disconnect here.

I think the discrepancy I would like to suggest is due to the Mizuta study which is relied upon by the ATSDR assessment and the EPA OPP for the short-term value.

And, in general, the short-term literature for arsenic is just not as good for defining dose response at the low end as is the subchronic and chronic.

And this is a shortcoming that I don't think we can really do anything about. But maybe we can use some logic to figure out what's the best course of action with that uncertainty.

Next slide. Let me just tell you about the Mizuta study. It is a soy sauce poisoning incident in, I guess, general

population including children and other people. There were over 400 cases -- 417, I believe. 220 are reported in his paper.

For some reason, he doesn't report anything about children. I don't know if they didn't observe any effects in children or they just weren't as severe. But the youngest age he reports is age 14 or 15. And I just want to point out that, because the soy sauce concentration of arsenic is extremely high -- it's 100 milligrams per liter -- that small differences in intake or even small uncertainties in the concentration could have huge consequences for the dose that some of these people got, and I think Bob pointed this out.

But I just wanted to show you as an illustration that 30 mills is not really that much soy sauce for a Japanese person in 1956. They probably had a very traditional diet. And from my observations in three trips to

Japan and looking at my relatives, including my six-year-old son, 30 mills is only this much, which might be a good long-term average, but even for my son, he can eat more than this in a day of soy sauce. I'll just pass this around.

So you can see that if you have a little more than two tablespoons per day, you soon have a much higher dose than the .05 milligram per kilogram per day.

Also keep in mind, if there were women or younger children, they are going to have a much higher dose per body weight, and this is what we always look at, dose per body weight. And keep in mind that any drinking water studies, when you have a large population exposed, often the dose is calculated for sometimes up to ten years of age or an older person like an adult. But really the kids in that same population had a much higher dose per body weight because of their greater

intake per body weight.

Next slide. So I think what I would like to propose is that we look at the greater arsenic literature and try to ground-truth the estimates and figure out where that lower bound for acute or subchronic or short-term might be.

And when we look at the literature, as Bob pointed out, you have the leukemia treatment studies where this is very controlled dosing, and so it avoid bioavailability, it avoids any uncertainties in dose. It's pretty tight.

And what we see is that even higher doses of arsenic do not cause the severity of effects seen in Mizuta. Now, you wouldn't expect the gastrointestinal effects because it's IV, but still, it just causes some question in both Mizuta, et al., 1956, and Franzblau and Lilis.

I think the more substantial

literature is the multiple subchronic studies involving thousands of people, including children, and most of these populations were malnourished. Many individuals in there were malnourished.

So those studies support, as Bob reviewed, a subchronic LOAEL of about .05 to .06. It's very similar to the subchronic LOAEL or the short-term LOAEL you get out of Mizuta, et al. So you know that that short-term LOAEL probably is a little low.

Next slide. Basically, again, short-term effect levels should not be higher than long-term effect levels -- it should be higher -- I'm sorry. The reverse should not be true. Short-term effect levels should be higher than long-term effect levels.

There is a poor database, as I told you about, for these short-term studies. They are mostly poisoning incidents, case reports. Dose information is very uncertain.

The subchronic and chronic studies indicate that factors of 10 -- two factors of 10 are too large for a margin of exposure. And certainly the subchronic information that Bob presented indicates that a factor of 10 is too large to go between the NOAEL and the LOAEL.

Next slide. Just some recommendations. Maybe consider setting a lower bound for short-term LOAEL and the margin of exposure using the larger arsenic database on longer term exposures.

That the uncertainty in Mizuta, et al., for the severity of effects noted is probably in the direction of an underestimation.

And this additional factor of 10 for severity of effects for Mizuta, et al., in the end is probably unnecessary, based on the greater arsenic literature.

Now I want to talk about dermal, and

just some general comments to try to ground-truth dermal.

Next slide. Now, I'm not saying that the dermal pathway is insignificant. In reality, we don't really know. But what we do know is it is probably not very significant compared to the oral, just based on what we know about how metals behave with the body and how anything that affects solubility of metals at the skin surface is going to be more dramatic than in the gut, I would think, because there are no digestive processes, there is no pinocytosis going on at the skin, there is no -- low, very low pH environment compared to in the stomach. So these metals are not fat-soluble and they don't easily cross the epidermis.

I mentioned the bioavailability, that bioavailability should really have a big impact on dermal, even bigger than oral, and that the relative contribution of dermal to

total exposure should be relatively small compared to oral. This is suggestive evidence that tells us this.

Yet, when we look at the proposed exposure assumptions -- let's see the next slide -- dermal is a considerable part of that exposure. And this is just an example that shows you -- we just kind took some numbers from the available literature to compare apples and apples.

So we have the same amount of residue on the wood and just focus on the yellow and the light blue. Dermal is in the light blue. Wood residue, dermal. Yellow is the ingestion. Upper pie is central tendency. Dermal is bigger than oral, using EPA assumptions for intake.

And then in the high end of the pie, you see that dermal is still a sizable fraction, maybe 25 percent, a little less, than oral. But the high end has some pretty

high mouthing behavior assumptions.

Next slide. So I thought, well, let's look at what do we know from biomonitoring? Urinary arsenic levels have been suggested by this committee as one way to look at what kind of exposure is going on.

What we have is not CCA residue biomonitoring data, but we do have some pretty good paired environmental and urinary arsenic data on 364 children from Anaconda, Montana. And that's arsenic in dust and arsenic in soil and maybe even some -- I don't know if they have -- I think they had some water, too, but that was very low.

Basically, region 8 scientists and their contractors compared the EPA soil ingestion estimates for the central tendency in the upper percentile to the central tendency in upper percentiles of speciated arsenic observed in the urine of these children. They assumed a 100 milligram per

day soil ingestion rate for the central tendency, 200 milligram per day for the upper percentile soil ingestion rate, around a 20 percent bioavailability factor for arsenic.

And what they found was they got pretty good prediction of the central tendency for speciated arsenic in urine. They tended to overestimate the upper percentile, but they were close.

So this is reassuring that, with soil ingestion, you could capture all the exposure. What Walker and Griffen didn't realize maybe at that time was that they were actually overestimating the amount of urinary arsenic that was due to soil ingestion and dust because they didn't account for the dietary contribution of inorganic arsenic to urine.

Next slide. As we see here, what you see as a total observed dose from the urine is a combination of what you get from soil, dust, food, water and air. Now, water and air are

probably, for this population -- well, water was accounted for. Air was probably insignificant. But food can provide several milligrams per day of arsenic.

So actually, the soil ingestion assumptions, the Superfund soil ingestion assumptions probably overestimated exposure.

But what this is telling us is if dermal are significant, what I would have expected is that the soil ingestion and dust ingestion numbers should have underestimated what we actually saw in the urine, but that didn't happen.

So however much dermal is being -- how much arsenic is being absorbed dermally -- next slide -- the oral intake estimates are more than adequate to account for any dermal exposure.

Now, you might ask, how does that relate to residues?

Well, we have kind of a similar

situation. The mechanism is the same. In both cases, children are touching residues, absorbing it through their skin, I guess, however much, and they are also engaging in hand-to-mouth behavior that's resulting in ingested arsenic -- particles in the arsenic.

So we know that the behavorial approach EPA chose to use results in quite high mouthing behavior. And if -- soil ingestion is pretty high.

So I'm pretty comfortable that probably the oral route should more than account for what is dermally absorbed.

And maybe this is why certain regions like region 8 -- I think Bob will talk about this later -- they do not quantify the dermal pathway.

Now, you may feel that you need to do this just to check on it. But I think when you get your final assumptions and estimates and the amount of contributions, you should

kind of consider that in your mind when kind of ground-truthing that with what we know from reality.

Thank you very much for allowing me to comment.

DR. ROBERTS: Thank you. Are there questions?

I'll just go down the line. Dr. Chou, Dr. Mushak, Dr. Francois, then Dr. Morry, and we'll work our way up this side.

Let's start with Dr. Chou.

DR. CHOU: Dr. Tsuji, you presented some very fundamental, very basic toxicology principles at the beginning of your talk. You show the toxicity values of acute, subchronic and chronic and their relationships.

You seem to not understand why the subchronic toxicity value can be reversed with acute toxicity values.

It's a wonderful thing -- arsenic is a very toxic chemical, we know. Are you aware

that one can be protected by exposing low levels of arsenic chemicals through long-term and then you can give a huge dose and a person can take it?

This is also showing a lethal dose in humans is a wide range from tenths of milligrams to thousands.

So there is adaptation to the arsenic.

DR. TSUJI: So your question to me is am I aware that you have adaptation to arsenic when you have repeated dosing? Yes, this is true, although --

DR. CHOU: Wouldn't that give you a reverse relationship to acute and subacute toxicity values?

DR. TSUJI: I guess that adaptation -- I don't think the adaptation is as much as you're suggesting, that it would reverse the order of expected toxicity.

I would assume that even the people that started out -- you know, even if they are

having some adaptation, it would -- you know, if they are having severe effects, the effects, for example, that were noted in Mizuta, et al., those people wouldn't have been continuing to drink that water to the point where they had adaptation. They were already having health effects, so you are going to see those health effects -- for example, in neurological, were irreversible.

So I understand what you're saying, and it does play a role in arsenic toxicity, but I think the amount of adaptation with chronic exposure is not to the extent where it's going to reverse that order.

DR. CHOU: We don't know the actual exposure at that time, but it is reasonable to assume the beginning of exposure varies between individuals --

DR. TSUJI: I totally agree.

DR. CHOU: So those that consumed at the beginning, they would be more resistent to

the exposure later.

DR. TSUJI: I would agree that we don't know a lot about what people are exposed to, particularly in the Mizuta, et al.

I would like to also submit that in 1956, the Japanese had a fairly traditional diet with a high amount of rice. Rice has a fairly large proportion of inorganic arsenic, so I think there have been various papers in the literature showing that such diets do contribute quite a bit of dietary arsenic, more than you would expect, for U.S. populations.

DR. CHOU: Wouldn't that make that population more resistent to arsenic toxicity?

DR. TSUJI: No, I would think that would make them more susceptible, because they are already having a high dose of arsenic.

I guess with your comments about resistance, I don't know if that -- you are almost implying that one should consider that

for chronic exposure to treated wood as well. I mean, the diet and -- we're talking about additive exposures, and yet you're -- I mean, the two are not connecting in my mind. Maybe I'm just having problems.

DR. ROBERTS: Dr. Mushak?

DR. MUSHAK: Two quick questions, Joyce, the first one regarding the potential for urinary levels in screening, the lowball uptake rates.

Yesterday, I tried to corner Professor Aposhian with this problem of biliary clearance, and Professor Styblo this morning brought that up again.

To the extent that we don't really know what the proportionality is, biliary versus urinary clearance, isn't it the case that all urinary levels are low estimates of what probably the best estimate is? That's one.

Two, could you comment on the fact

that the academy reports on the malnutrition as a factor in the Taiwanese population is probably a no-issue.

You seem to preserve the idea that they are a non-representative population on the basis of malnutrition. I think we've put that issue to rest.

DR. TSUJI: Let's just talk about these separately before I lose track.

You asked me whether urinary data are low estimates of exposure. And I know about biliary excretion of arsenic, but I have never heard anybody say the urinary estimates or the urinary measured data are low-end indicators. And I think they are -- that is the biomarker that everybody uses for arsenic exposure and it's one of the better ones we have. Now, it does reflect short-term exposure, within the last few days.

But, there again, in the case of Anaconda, when you have a large cross-section

of children, that should hopefully take into account daily variation.

But, you know, I haven't heard what you just said, that because of biliary excretion, that it would be the underestimate you're talking --

DR. MUSHAK: Well, absence of acceptance of biliary -- you know, has nothing to do with the popularity of a measure. I mean, all measures have problems. They all have limitations.

DR. TSUJI: Oh, sure. Yes.

DR. MUSHAK: So to say that no one has really brought up the issue of biliary clearances, I mean, that's an irrelevancy.

DR. TSUJI: Well, no one has brought up that urinary estimates are underestimates because of biliary excretion. I have heard people discuss biliary excretion --

DR. MUSHAK: But I think it follows, doesn't it, I mean, from basic toxicokinetics

of arsenic or anything else?

DR. TSUJI: It's complex. Dr. Steinberg mentioned -- there is also possibly intestinal uptake, too. I don't think we know enough, but I think we do have good information correlating to oral doses with urinary excretion rates. And I think maybe that's the way to check on whether biliary excretion is being -- is really affecting that relationship.

DR. MUSHAK: If you want the full magnitude of uptake, I mean, if the issue is bioavailability, you want to know all of the excretory pathways. If you simply want to answer the question is there excessive exposure, urine is fine. Those are two different issues.

DR. TSUJI: Your second question had to do with malnutrition. I know that the NRC 2001 update commented on whether -- I think what they were trying to put to bed is this

idea that because the Taiwanese population were malnourished, that's why they were having all those health effects. I don't believe that's true, either. It's clearly that they were having arsenic exposure, and that was probably the main contributing factor to the cancer rate.

What we don't know is to what extent malnourishment contributes to it. The NRC report felt that it didn't contribute enough for them to consider it. But on the other hand, we do have good data within individuals. For example, Mazumder has shown that if you are below a certain percentage body weight, you have higher incidence of skin lesions and other arsenical effects.

So on -- there are other studies that show that. On individual levels, severe malnourishment does cause sensitivity. So I wasn't raising malnourishment to say that, that in the sense that you are talking about,

that needed to be put to rest, that malnourishment explains all the arsenic toxicity we see in the world. I was just saying that we have included sensitive populations.

DR. ROBERTS: Before we go on with any questions -- and I will give you the opportunity to do that -- let me remind the panel, we still have lots of presentations coming from EPA today. We still have a very full schedule ahead of us.

So let me ask -- and I certainly want to give panel members the opportunity to clarify issues that have been raised by Dr. Tsuji, but let me ask the panel to keep in mind that we still have a lot ahead of us today and try and make this process as efficient as possible.

Dr. Francois?

DR. FRANCOIS: I just have a quick question. With so much resting on the Mizuta

study, it seems to me that the dose -- the estimated dose in that study is not really clear. And the authors themselves word it this way: They say the estimated dose is about -- and they gave us -- and it seems to me we all take this at face value.

What are your thoughts on that? Did you go back and try to estimate the dose from the amount that was excreted in the urine of the five patients that were reported?

DR. TSUJI: See, the problem is I don't think that would characterize the population of people having the effects, either.

I don't think the Mizuta data provide enough information to really get any better estimate, and I think the problem with all the acute short-term studies we have -- which are not really studies; they are case reports -- is that they don't quantify dose very well in the end. And.

That's the reason why we need to rely on the greater arsenical literature to help us try to bound the estimates and decide where should we start becoming concerned about short-term exposure.

DR. FRANCOIS: And there was no mention of food intake either, was there?

DR. TSUJI: No. This was all dose based on soy sauce. It didn't account for food. It didn't account for -- you know, there are a multitude of factors that could have been interplaying here, for example, the high salt content of soy sauce and the high salt content of the Japanese diet is irritating to the stomach. That could have combined to make the gastrointestinal effects worse.

DR. ROBERTS: Dr. Morry, I believe you were next.

DR. MORRY: The question I was going to ask is similar to what Dr. Francois just

asked about the Mizuta soy sauce study. It might be interesting -- he just sort of guessed how much soy sauce people were using, and you apparently have your own guess --

DR. TSUJI: Based on this, I would say it's an average, and it's probably not bad for a long-term average.

DR. MORRY: So it might be interesting if you would make your own estimate and just see how much that would change the LOAEL.

The other thing is, you said that rice -- the kind of rice these people were eating was probably high in arsenic. Could you be --

DR. TSUJI: Yeah. All the rice samples that have been measured in the literature show that the inorganic arsenic is relatively --

DR. MORRY: Could you be quantitative about that and actually determine whether the amount of arsenic that would have been added

from rice diet would have been significant compared to the amount that they would be getting in that amount of soy sauce?

DR. TSUJI: Yeah, that's a good point. You know, I haven't gone back and made that calculation. I do know from looking at Indonesian populations that having rice at every meal does increase your overall arsenic intake quite substantially over the U.S.

But you are right, they were getting an amount of arsenic in this soy sauce. So you are right, it may not have contributed that much. I haven't done that calculation.

And if you want to see the impact, I did some preliminary guesses, and I can't say that I'm any better, but just based on what I have observed people ingest and what I think might be possible, I did some dose calculations and I will leave Dr. Roberts a copy of my slides and you can look at those at your leisure and stick in your own numbers.

And who knows.

DR. ROBERTS: Other questions?

Dr. Steinberg?

DR. STEINBERG: I guess we should start out with some hard data and then we can go into speculations.

The leukemia studies that you quote related to effect of arsenic, there is no conceivable way that anyone can extrapolate data on patients with cancer who receive radiation, who receive chemotherapy, where they are not looked at closely related to their neurology, related to the effect on their nerves, related to the effect on other organ systems, related to the arsenicals. The oncologists never even dreamed of looking at that well and they don't look at that well. That was not the point of those studies.

No one can really extrapolate any meaning related to those studies with horribly sick people that are receiving such a large

overdose of other toxics who are also under cancer.

Regarding some of your earlier -- the picture characters related to your short-term versus long-term, you know, I love regulators, some of my best friends are regulators. However, I am not a regulator.

And, of course, I am cautioned to use the best science possible. And if I have a good mechanism of action -- and it looks at this point as we are very, very, very quickly evolving a mechanism of action on two fronts.

One front is, again, the direct interaction of arsenic with DNA. And, two, we now have about these 30,000 genes that exist in the human genome -- you know, in animals, we have the arsenite methyltransferases. You know, a lot of this data is fluid. And I'm going to be very worrisome -- I'm going to be worried about speculating on uncertainty principles when I have better science that may

tell me that there may be something awry and amiss.

Also, regarding --

DR. TSUJI: Wait a minute. Can I just start in because I'm going to forget what you said.

DR. STEINBERG: Why don't you write them down and then I'll finish my last comment. And then you can roll along and I'll try to stifle myself.

The third comment is I, of course, had sushi. I apologize to admit it. I weigh 55 kilograms. I have maybe even a touch less. I had 12 pieces of sushi last night. I had exactly 10 mill of soy sauce.

I recently returned from two weeks in Japan. I had the opportunity of watching my children over that two-week period. I think I can also speculate. I would tell you that the best guess that I could see is that there are no Japanese that I saw, and there was no one

else that I saw that's knocking off 30 mill of soy sauce, with a very good meal. So we can speculate on the other end also.

So, again, all of this open speculation is exactly that and it would be great for a quiz show or something else, but I don't know how pertinent it is here.

DR. TSUJI: Let me go in backwards order.

The soy sauce. There was probably a range in that population. There are probably people that eat less. I think I eat less than this. That seems like a lot to me except on certain days, I think I do eat this much, when you add up all the meals together. Maybe one sitting, 10 mills, okay. But when you add it up in the different ways they use soy sauce and the fact that, in '56 they had a more traditional diet, and just observing what my son will do who I have had to really severely cut back because he will drink it out of the

bowl, the silly kid.

DR. STEINBERG: All speculation.

DR. TSUJI: Yeah, you can speculate all over the place. And that's why I'm telling you to be very careful about hanging your gold standard on Mizuta and on that number and then citing that that is the only thing you can use.

I think -- and that gets into what you are saying about the science. I would encourage you to use the best scientific information available. In this short presentation I didn't have an opportunity to present anything else. You, obviously, have more, and the panel collectively has more experience that could bear on this issue that I can't present or have the experience to present in the 15 minutes.

So I differently encourage you to do that and not rely on simplistic, okay, let's find one number and then throw in a whole

bunch of uncertainty factors. Let's use the best science.

Regarding the leukemia study, I'm not saying that that is the gold standard either. All I was trying to point out is there we do have controlled dosing and you didn't see the severity effects to the extent of Mizuta. I'm not saying that they didn't have any effects at all or that that should be used as the study.

So I hope I didn't give you that impression.

DR. ROBERTS: Any other questions?

Dr. Kosnett?

DR. KOSNETT: Joyce, hi. I wanted to ask you -- you addressed the issue of margin of exposure with respect to severity of symptoms.

What would you suggest to us to consider a severe effect that would warrant a margin of exposure of 10 and what type of

effects, you know, relevant to the studies we're talking about do you think should merit a lower margin of exposure?

DR. TSUJI: If I thought the LOAEL, the .05, was directly correlated with the effects they were seeing, I don't see any problem with putting some margin of exposure in. But I think once you do that, you do need to back up and decide, well, am I getting below what we know about the dose response for arsenic? So using all available Science, what do we know about that?

In this case, I am very uncertain on whether the severity of effects seen in Mizuta, et al., are related to that .05. And so the whole severity issue, I think, should be set aside until you can decide where should we be in that dose. And use the more scientific approach to the whole --

DR. KOSNETT: Granted, and I think your point is well taken that we need to

carefully consider the dose issues in that study with respect to how much they were. But I'm talking, that aside, in your opinion, you know, EPA has a policy of putting margin of exposure depending on the severity effects.

And what I wanted to ask you -- you know, you have studied this issue. What is your feeling about what margins of exposure should be used for what severity of effects? I mean, we have things like prolongation of Q-T intervals, we have nausea and vomiting and diarrhea, we have peripheral neuropathy.

From your perspective, what is a severe effect and what merits a ten-fold margin of exposure and which ones are not substantial and don't merit a margin of exposure and which ones fall in between?

DR. TSUJI: You know, you are right. The margin of exposure -- EPA elsewhere has said that it can be anywhere from 1 to 10 and then you can have multiple factors. And I

think what you also need to consider is, you know, how severe the effects are, but what do you know about the dose response curve? For arsenic, it seems rather steep. So in some cases, there isn't that much difference between having severe effects and having less severe effects.

In some cases, I don't think there is a full factor of 10, it appears, (ph) between, for example, the NOAEL and LOAEL that Bob was looking at.

So I guess I don't have a perfect answer. And I certainly can't give you an answer for -- you know, any answer I give you has to be specific for a chemical. In this case, arsenic, I think it depends on the type of effect you are leaking at and, obviously, neurological is much more severe than acute GI symptoms. But I think you have to take into account the shape of that dose response curve and what you can see about that.

DR. ROBERTS: I think we need to move along.

Thank you very much, Dr. Tsuji, for your comments and your answers to our questions.

I have one other public commenter listed, Scott Conklin, who is with Universal Forest Products, Incorporated.

Welcome. Could you please introduce yourself to the panel.

MR. CONKLIN: Good morning. My name is Scott Conklin. I'm the director of wood preservation for Universal Forest Products. Let me start by saying that had I known I was going to address the panel, I would have brought a tie on this trip, so I do apologize.

Yesterday, EPA gave you a very good description of the treating process. However, in questions, I think EPA was asked to get into some kind of levels of detail that those of us in the industry thought we might be able

to help clarify. So that was the purpose of asking for a couple of minutes to address the panel.

There were three principal things that I wanted to try to clarify. One was -- you were asking about the different times of CCA, CCA types A B and C. There was a question related to the use of final vacuums in the treating process. And then a fairly specific point to make about fixation.

First, starting with types A, B and C, types A, B and C represent an evolution of the CCA formulation. And that evolution was working to improve the efficacy of preservative and minimize leaching from the product.

Type C was introduced in the 1960s and effectively type B replaced type A; type C replaced that. So it was introduced in the late '60s.

Today, there is only type C. There is

no type A. There is no type B used in the United States.

Our best estimate -- again, it was introduced in the '60s. Pretty well, people went over to that. I can say with confidence that there hasn't been anything besides type C used for over 20 years.

Second point -- so I guess the bottom line is it doesn't seem to me that that's really going to play a role in your deliberations. You have plenty on your plate and you can probably take that one off.

A question was asked about final vacuum in the treating process. The process used is a vacuum -- pressure vacuum process. Pretty well always has been. Wood species and some other factors affect how much liquid preservative, how much treating solution is left in the wood at the end of the process.

The point I wanted to make -- and in some types of wood, the treater has the

ability to play around with that through other parts of the process, of how much liquid, how much water I'm going to leave in that wood.

The point I wanted to make was that it does not affect the amount of CCA left in the wood.

If I set the process up so that I'm going to leave three gallons per cubic foot in the wood, I use a lower solution strength because, as a treater, I want to put in exactly what the standard calls for, no more, no less.

So while final vacuum is out there, it probably really, again, isn't relevant to the things you are being asked to address.

Third point on fixation. The main point I wanted to make here is that fixation is not a separate process. In our treating plants, we don't have to go from the treating process and say, okay, now let's do the fixation process.

Fixation is, as you have heard a couple times now, a chemical reaction where the preservative binds with the wood. It is a time, temperature and moisture-dependent reaction. That fixation process starts immediately when the treating solution comes in contact with the wood.

In work that we have done in our company -- and I think this is pretty well documented in the literatures as well -- literally right out of treating cylinder, you are already at about 60 percent because, again, this chemical reaction starts immediately.

Also, in terms of -- some points have been made about cold weather. And, again, it is -- the length of time that it takes to go to completion is dependent on temperature. Warmer temperatures, faster reaction.

But even at temperatures as low as 5 degrees Fahrenheit, fixation will still occur.

It's just that it's about ten times longer than at 37 degrees Fahrenheit. So, again, what's going to happen is the amount of time is going to change. But that reaction will still proceed.

Just very briefly two other points that came up later in the day. There was a question about sealants. Let me just try to clarify what the industry position has been on sealants.

Sealants have been recommended since the late 1980s. And, again, it is for aesthetic reasons to reduce checking and splitting of the wood. Then, in the mid 1990s, the industry introduced a factory-applied water repellant which is incorporated right into the treating solution and pressure applied to the product.

The benefit of that was that it allowed consumers to go a year to two years, depending on the water repellant, the product

you were talking about, before they had to go, in order to follow our recommendations, and apply another layer of water repellant.

Final point is on wood chips. I don't want anyone on the panel to misunderstood that the wood chips that are used as a buffer in play areas, these are not CCA-treated wood chips. Wood chips are not treated by this industry. By nobody in this industry.

In fact, the only instances we have ever heard of the idea of a treated wood chip actually came from Florida out of Dr. Solo-Gabriele's work and Tim Townsend's work where they were talking about material being brought to a landfill ending up getting chipped up as mulch.

Now, this is both infrequent, a violation, as I understand it, of Florida regulation, and something that's absolutely not supported by the treating industry.

So -- and we have talked about it

before. We are happy to do whatever we can to minimize that happening. But this is -- treated wood chips are not a product that you find out there in the marketplace. Thank you.

DR. ROBERTS: Thank you, Mr. Conklin.

I believe Dr. Solo-Gabriele has a question for you.

DR. SOLO-GABRIELE: Before I get to the wood chips, I had a question about fixation.

It's my understanding -- I'm not a wood treater. It's my understanding that you can allow natural processes to just air dry it. But there are some wood treaters that do undergo an extra step such as kiln drying, it's my understanding. Is that --

MR. CONKLIN: There are some folks who do that. We're talking about a very tiny fraction of the industry. It has been predominantly used on poles. There are literally one or two treaters.

I mean, in terms of a percentage, you are talking about well under 1 percent of the industry that's chosen to do that.

To be honest with you, you know, we know what happens when you leave the wood alone. There is information that says -- and you can use kiln drying to speed it up. One of my concerns has always been that if you don't do the kiln drying right and you dry the wood prematurely, you can actually -- I'm more concerned that you can mess up the process.

You can use it to speed it up, but it's a very, very tiny fraction of the industry that actually does that.

DR. SOLO-GABRIELE: But there are these processes that exist that can be included.

Getting to the issue of wood chips, a lot of our work has focused on the wood material that comes from construction, demolition recycling facilities. We analyzed

13 different facilities throughout the State of Florida. And in 1996, the average content of CCA was 6 percent.

We went back out in 1999, three more facilities, and we found that the concentration of CCA within those piles was anywhere from 9 to 30 percent.

We have taken samples from retail establishments, found that they leach arsenic above levels, indicating that they do contain CCA.

We have received samples not only from Florida but we've received samples from other states as well. And they show evidence of CCA in the mulch. So it's getting everywhere. And it's getting very hard to control.

MR. CONKLIN: Well, again -- I guess the main point was that this is not a product that anyone in the industry would support if it is inadvertently getting into the much stream. I mean, you have done a lot of work

on identifying that in the waste stream and trying to help control that. And we're absolutely supportive of that work.

DR. SOLO-GABRIELE: Yes, but when you state that it's insignificant and it's not happening, the data is overwhelming the other way, that it's getting into places that it should not be.

DR. ROBERTS: We have several more questions.

Again, let me remind the panel, we have -- after we finish the public comments, we have three-and-a-half hours of presentations left today before we begin our discussion. If there are comments that you want to make and they can fit into our discussion of the issues when we get to those, please hold them until then.

Dr. Styblo?

DR. STYBLO: I think this is an important question. I'm still confused about

the chemistry of the treatment. We heard yesterday and today again that this is a complex redox reaction in which chromium is reduced from 6 to 3 and, for some reason arsenic, stays pentavalent and copper stays oxidized.

By definition, chemical redox reactions involve two kind of processes and at least two components. In this kind of reaction, one component is oxidized; the other one is reduced.

Because there is a concern about residual copper 6 in the product -- or in the leaching substance, could you explain what exactly reduces chromium from 6 to 3 in the process?

MR. CONKLIN: Well, I am a chemical engineer and not a chemist. So the one thing I can tell you is that it is well understood and very well documented in the literature that the order of materials locking in of

fixation is that the copper and arsenic locks in first, and that the last thing to go is the conversion -- is the complete conversion of the hexavalent chromium. That's why there have been test methods established in the industry that look for hexavalent chromium.

And in all of those test methods, they indicate that the presence of hexavalent chromium is not there after the fixation reaction is complete.

And whether it takes, you know, three days or two weeks -- certainly wood that is out there in service for any period of time, all the data I have seen says that that hexavalent chromium is not present.

So I'm afraid I really can't answer the question you are getting to except to say that the hexavalent chromium does not appear to be there in the finished product.

DR. ROBERTS: Drs. Gordon, Francois, Smith and then Ginsberg.

DR. GORDON: I'm curious about the fixation, the speed of fixation. You said that as soon as it comes out, it's 60 percent fixed, meaning it's reduced -- the chromium is reduced. But unless I read the McNamara papers or reports incorrectly or my memory failing, which is more likely, I thought that he had, for the first three days, what he squeezed out, which is different than what you probably measure -- but what he squeezed out was predominantly hexavalent for the first three days, and then within a week, it dropped below detectable levels.

But regardless of that, what is done -- I mean, what's on the outside versus what you take as a core -- I mean, how do you know? We're all sort of interested in what is the speed of fixation in winter versus summer, if you can do it succinctly?

MR. CONKLIN: Well, again, the only thing I can tell you is that there are

quantitative measures, and I have done work -- in fact, I have done work in Jamesville, Wisconsin, in the dead of winter when it's about 10 below outside. In that work -- and it's been repeated a few times since then -- I regret that it hasn't been published -- what I was finding was that right out of the treating cylinder, I was right around 60 to 70 percent fixation and, even in those conditions, was going to complete fixation in a short period of time.

So I would have to go back and read Dr. McNamara's paper to try to really answer your question. But I can tell you that based on the work that I have done, that's about where you are coming right out of the cylinder.

DR. ROBERTS: Dr. Francois?

DR. FRANCOIS: We heard yesterday that there is a relationship between the amount of leaching that you can get and the fixation,

that there is a relationship there. And as you mentioned that right out of the cylinder -- right out of the cylinder the fixation rate is about 60 to 70 percent.

And, therefore, my question is, since it's a time-dependent process, how long is the treated wood -- how long does the treated wood stay in your facility before it's shipped out to be sold to consumers?

MR. CONKLIN: I'm glad you asked that question because, from some of the conversations yesterday, I was wondering if maybe people had this impression that it comes out of the treating cylinder and, two hours later, it's sitting on the store shelf, which is not the case. I can tell you, from my own company, we have minimum holding requirements of 24 to 48 hours before it's moved to outside storage.

So, typically, you are looking at probably on the earliest end, three to four

days after treatment where it could possibly be on a shelf, and that would be very infrequent.

More common is that it sits in my plant for weeks to months in inventory before it ends up on that store shelf.

So I hope that answers -- and to some extent, that answers -- Dr. Solo-Gabriele pointed out that there are some people who have gone to the much-added expense -- I won't bore you with why it's so expensive, but just trust me, it's very expensive to do something like kiln dry after treatment to force fixation.

And the only reason someone would do that is if they wanted to try to shorten that time frame and try to bring it to market -- and to try to bring it to market sooner.

DR. ROBERTS: Dr. Smith?

DR. SMITH: Thank you. I just want to make sure I have the dates correct here that

you gave.

You said it was basically around the 1980s that the industry began giving its general recommendation of sealing the wood with some sort of sealant every year or two years. Is that correct?

MR. CONKLIN: Yes. We kind of did a huddle-up yesterday, and that was our guess was that probably mid-'80s or so when those recommendations started.

DR. SMITH: And did you generate any of your data on the efficacy of different sealants in helping to prevent this sort of cracking or other sort of -- what you describe as aesthetic concerns with wood?

MR. CONKLIN: That work is basically done by the registrants, by the CCA manufacturers.

And as a treater, I would say yes, but I couldn't quantify for you. And, again, what they were doing was looking at, if you applied

these things, that you -- the mechanism for causing checking and splitting is that wood in an environmental situation goes through cycles of wetting and drying. And by putting a sealer, you are trying to minimize its uptake and, therefore, try to smooth out those cycles that it's going through.

DR. SMITH: But it might be possible for you to inquire with your colleagues about whether or not you have any data on the efficacy of different sealants in this checking, cracking --

MR. CONKLIN: We can do that. Should we come back to you on that?

DR. SMITH: Yes, or EPA or whoever. I think it would be interesting to know if you have any data on that.

Also, what was the date that you said that you began adding some sort of pretreatment into the actual fixation -- or the process itself?

MR. CONKLIN: Right now, it's a very small portion of the market. It's probably something like 6 percent of the CCA-treated wood market has a factory-applied water repellant. Those were really introduced into the market in probably the mid 1990s, but continues to be kind of a specialty product.

The vast majority of material that you are talking about out there does not have a factory-applied water repellant. It's expensive, it's kind of an added thing that you can buy.

DR. SMITH: And why is it that -- and at least this is my understanding of it, and perhaps I have it wrong. What's the recommendation to builders and consumers to wait a certain amount of time before applying sealants?

MR. CONKLIN: That goes back and forth. My own recommendation is that they can apply that within 30 days or so. And all you

are really trying to do is give the water -- when I treat wood, I'm basically taking -- the treating solution is 1 to 2 percent CCA; the rest of it's water. So I'm taking this wood and I'm basically filling it up with water. And it's probably just a little more effective, particularly if you are talking about a paint, to -- you want to let that water get out.

We have done some work with just topical sealers that says, probably doesn't make a huge difference, particularly if you are not sealing the whole board. You are just sealing the top surface of, say, a deck board, so you're allowing the bottom surface that's still unsealed to continue to dry. But my standard recommendation is give it 30 days or so.

DR. SMITH: And my last question, if I may.

So am I correct that it is the

industry's conclusion that sealants are an effective way to reduce this sort of checking and cracking of the wood, since you seem to be making recommendations?

MR. CONKLIN: Yes.

DR. SMITH: So it is your position that it is an effective way to reduce that?

MR. CONKLIN: Yes.

DR. ROBERTS: Short questions, please, from Ginsberg, Solo-Gabriele, MacDonald -- Dr. Steinberg and then Dr. MacDonald.

DR. GINSBERG: I think that the issue of how long one should wait, the 30-day waiting period you just described is very germane to any -- if there are any recommendations coming out of this committee regarding sealant use, the proper way to do it -- it would be helpful if there was any data, if you actually had any studies along those lines, it would be very useful for us to see.

And the other point you sort of didn't think was very germane to this discussion, but I think it is, and that is the CCA-A and CCA-B which I was asking about yesterday, and thank you for clarifying the time frame for that.

But if one goes out and does a random study of decks or playscapes and some are old and some are new and you are going to be introducing some variability, then, into your results, it sounds like, because the arsenic content of these different formulations was different, as EPA presented yesterday, and you are saying that if something is beyond, say, 1970 in age, there is a pretty good chance that it had some other formulation.

I had done a little bit of background reading on this. Maybe you can answer this question. Was the fixation of the materials the same as CCA-C? Is there a greater or a lesser potential? Maybe it's just an impression I have that there was a greater

potential for leaching or less fixation or something along those lines with these older formulations. Is that accurate?

MR. CONKLIN: Well, let me first tell you that the reason I think that it's probably going to be insignificant is that, if you think about it, everybody didn't have a deck in the back of their house in 1970.

The popularity of decks also traces a huge increase -- essentially, the industry that I am in, which is the residential treated wood components, as opposed to utility poles and railroad ties, that pretty much started in the 1970s in any significant way.

And I'll tell you the industry enjoyed tremendous growth through the late '70s through about the mid-'80s. I have to tell you it's been dead flat since then. The market has not really increased or changed in size. It's been a flat market since then, basically. But that's really when it

happened.

So part of why I said hat I thought it would be insignificant is the combination of that time frame that it was introduced in the '60s, was pretty much the thing in the '70s, which is when people started building all these decks. So you might hit one. I honestly think it will be pretty rare.

I do think you are right in saying that those earlier formulations probably were not as well fixed. That was one of the things that they were working on as they evolved it, was modifying the formulation to get the right balance and to improve the fixation.

DR. ROBERTS: Short questions, please, from Solo-Gabriele, Steinberg and MacDonald.

DR. SOLO-GABRIELE: I just wanted to reiterate Dr. Ginsberg's request for some data on the fixation process, the time, moisture and the temperature effects, if there is a way to get some of that published information.

It's my understanding that there are some published studies on that, but I don't know if we can get it before the end of the meeting.

MR. CONKLIN: To be honest, I would have to ask somebody else. I mean, the stuff that --

DR. ROBERTS: We'll treat that as sort of a general call for information. If there is anyone in the audience who can respond to that and provide the panel with information in a timely fashion, that would help our decision process.

Dr. Steinberg?

DR. STEINBERG: If we could also get some more information on other resistent woods and other treatments, for example, the ammonium-chromium type treatments, as potential alternatives to CCA, I think that would be very helpful. I would love to see a menu of what else is out there and what else can be used.

Also, I would love for someone to be able to comment from the industry on an economic impact of some of these things. And I think, you know, if we're looking at a $7 billion square foot market of wood and, for example, in only playgrounds, 50 million square feet, which may be a small part of that, that may be consideration that I think people around the table may be interested in hearing.

Also, any further protections that you can think of or come up with, in particular as it relates to woodworkers and hobbyists who somehow fall into these things, I would also be interested in hearing. You can supply that information at any time.

DR. ROBERTS: We won't put all that burden on your shoulders, but we'll consider that a general call for information.

Dr. MacDonald?

DR. MacDONALD: The SCS hand-loading

study showed more than twice the arsenic concentration with the water repellant CCA-treated than with plain CCA-treated. Is this information consistent with the industry's point of view on the water repellants?

MR. CONKLIN: Well, I tell you, I think that that was -- the first time I had ever seen that was in the SCS data. I don't believe anyone else has done a similar look, and so that was very interesting data.

We have spent some time talking about those results, and we think it is probably related to the nature of the water repellant. When you treat with a water repellant, you are more likely, we think, to have some of this waxy material loading up on the surface, you know, initially.

So we think it's probably an artifact of that process. It is probably very temporary in that, in the longer term, those

things may end up getting reversed because you are not dealing now with whatever was on the surface initially. You are looking at what's there four months, five months, ten months later, which will probably be as much driven by the behavior of the wood out there.

So I'm not sure that that is a long-term -- that you are going to see that in the long term, but that was the first time we had seen that.

And, again, that was part of what I wanted to point out, that was a fairly small portion of the market, probably about 6 percent of the treated wood market.

DR. ROBERTS: Thank you, Mr. Conklin, for your presentation and your comments.

Before we close the public comment session of the agenda, I will ask if there is anyone in the audience, any other public commenters that would like to address the panel. This would be your last opportunity to

do so as we move further into to the agenda.

Anyone else? I see a hand. Could you please come forward, identify yourself.

MR. TURKEWITZ: I'm Rob Turkewitz. I'm an attorney in Charleston, South Carolina.

One thing -- and I'm not an expert in this area, although I have read as much as I can over the last couple of months. One thing I'm concerned about -- and I share a concern by the woman who addressed the panel from Florida -- and that is whether the panel or whether the EPA outlook is maybe underestimating the potential risk, and that is -- again, in Charleston, South Carolina, we have a longer period in which children play on playsets. And, also, we have a very hot and humid environment, and I think that may be something that ought to be taken into consideration.

I also want to mention one thing. And one of the things that brought this to my

attention was a friend of mine who is a veterinarian, and it's kind of an interesting thing that happened with him, and I'm sure a lot of you here have heard of situations like this.

Here is an individual who is very learned and actually knew that there was arsenic used in the treatment of the wood. He was building -- I think it was a playset for his children. And he took the wood afterwards that was left over and he burned it in the middle of his field and he had goats that his children had as pets. And the goats went in there and licked the residue, the ashes, and they were dead the next day. And he did an autopsy on his own goats and found out that they were poisoned from arsenic, and that's how they died.

And the interesting thing about that is why did the goats lick the arsenic residue? And that's just something that I wonder if

this panel has taken into account. And that is, I was told by my friend that he believed that it was a sweet, salty taste to it.

And that would be something that perhaps the panel ought to consider is whether or not there is a taste involved with the arsenic that's used on the -- that's on the surface of the wood and whether that would actually result in children putting their hands in their mouths even more than what the current estimate is.

Those are my comments.

DR. ROBERTS: Thank you. Are there any quick questions from the panel? Dr. Shi?

DR. SHI: My question is, are you aware are there any requirements to put a label on the wood? For example, this is toxic or arsenic-treated or something, to warn people this is toxic or dangerous? Are you aware about that?

MR. TURKEWITZ: Actually, I'm not

right now aware of any requirements as far as a label. It's my understanding that it was a voluntary requirement that's in place right now.

And I also -- I mean, I have seen -- I have been to Lowe's and Home Depot and I have seen the literature that's being put out, like by Universal Forest Products, where they actually say that it's perfectly safe for children in playsets and that the arsenic is locked in. And I may have a copy of that. I can distribute that if you'd like to see it. They say that the arsenic is locked into the wood. And what I'm hearing in the last two days is that may not be correct.

DR. ROBERTS: This may be an issue, if it comes up later in our discussions, that the agency can clarify for us in terms of labeling requirements.

Any other questions? If not, thank you very much for coming forward and making

your comments.

Is there anyone else who would like to make a comment before we close the public comment session? Last chance.

We'll then close the public comment session. Let's take a 15-minute break, and I mean a 15-minute break.

(A recess was taken.)

DR. ROBERTS: As we reconvene, there was apparently one additional public commenter that was here, has been invited at the agency's request, and we wanted to be able to accommodate that individual.

So before we begin with the agency presentations scheduled for today, I would like to offer the opportunity for Dr. Lamm to speak.

Dr. Lamm, are you ready to go?

DR. LAMM: Yes, I am.

DR. ROBERTS: Could you please identify yourself for the panel.

DR. LAMM: Yes, I will. Thank you very much, Mr. Chairman.

My name is Dr. Steven Lamm. I'm a physician epidemiologist. I've been in the private practice of epidemiology for over 20 years. I was formerly with CDC, with the Epidemic Intelligence Service. I have no experience with anthrax. I was formerly the senior epidemiologist at the National Institute of Child Health and Human Development and I am on faculty in the School of Public Health at Johns Hopkins, associate. I am full professor at the Uniformed Services University for the Health Sciences in biometrics and biostatistic -- for preventive medicine and biostatistics, biometrics. And I am associate professor of pediatrics at Georgetown.

I have been interested in arsenic for over 20 years, having started off in 1977 when I did the medical examinations of the smelter

workers in Anaconda. I am an occupational health physician, in addition.

Arsenic and benzene have been the two chemicals of greatest interest to me as an epidemiologist because they are the two chemicals for which there is no decent animal model and, thus, the question of assessing the risk from exposure has to be related to epidemiology, which for me is a pleasure.

My reason for speaking today -- I have two. And both of them I have in documents which I had prepared and which I have submitted to you, and hopefully are being distributed.

Back in 1984 I did a quantitative risk analysis on the issue of skin cancer risk to children who played on arsenic-treated wood in playgrounds. This was done at the request of an industrial group and was presented to the California Health Department in their deliberations at that time. I have given you

a copy of that report with all its typos and so on in there, and that's one thing I would like you to have for your consideration.

Since then, I have expanded the research work that we have done on arsenic. We have two major projects. One which we have brought to completion is our study of skin cancer in inner Mongolia and its relationship to arsenic in the drinking water. It is an unique study in that it is an epidemiologic study rather than an ecological study. That means we have an individual exposure history on each of the people exposed and we have an individual medical examination of each person.

The results -- that study has been presented at the International Conference on Arsenic and Health. Its analysis was funded by the ATSDR and is in press at the present time.

The findings of that study are, for a population of over 2,000 people exposed at

less than 150 ppb, there was an absence of skin cancer.

For those exposed above 150 ppb, micrograms per liter, there was an excess of skin cancer.

These data are consistent with the threshold hypothesis and reject -- are sufficiently strong to reject the linear hypothesis. There is statistically significant deficit of skin cancer in the group with exposure at less than 150 ppb. That is point one.

Second, we became -- as we were preparing this for our final report for ATSDR, we became aware of the work going on at EPA and the National Research Council, became interested in that and decided to give that a closer look.

If you will turn to my document that's written as a letter to you --

DR. ROBERTS: We may not have that

yet, Dr. Lamm. We are still trying to get this material -- some panel members have it and some don't. We're trying to get some copies made.

DR. LAMM: I understand.

I am making -- I have not read your materials. I am making the assumption that your risk analysis is based on analysis of the Southwest Taiwan data set. Am I correct in that?

DR. ROBERTS: No. It's actually more on the exposure and non-cancer issues that we're dealing with in this particular session.

DR. LAMM: Then my comments are related to the issue of cancer effects.

On that, with respect to the carcinogenic assessment of arsenic -- excuse me -- of internal cancers within ingested arsenic, the major point I wish to make is that the Southwest Taiwan study is an inappropriate marker for U.S. exposure.

We now have studies which are in -- have been submitted to the literature for review, which we had submitted to the National Research Council, in which we asked whether the type of ecological study that was done in Taiwan could be done in the United States.

We have, using data from the U.S. Geological Survey, identified 133 counties who use well water as their source, whose well -- excuse me -- groundwater as their drinking water source, whose analyses of groundwater is well-known by the U.S. Geological Survey.

Based on that, we have identified the median exposure level which fall in the United States between the range of 3 and 60 parts per billion. And we find that there is no change in the bladder cancer rate throughout this range.

The Taiwan study includes 300,000 person years of observation among people exposed to less than 400 parts per billion.

Our study includes -- is based on 75 million person years of observation among groups exposed to between 3 and 60 parts per billion, micrograms per liter.

The exposure data come from the U.S. Geological Survey. The outcome data come from the National Cancer Institute report on county-specific mortality rates by cancers for 1950 to 1979.

The results of those reach for us the conclusion, and a conclusion consistent with the rest of the population-based mortality studies, showing no increased risk of internal cancers at exposures less than 100 or less than 50 or 60 parts per billion.

This may be explained either on the basis of a threshold model or on the basis of some confounding exposures, particularly occurring within the Southwest Taiwan.

I will stop there since I have probably used up my time, and I thank the

chairman and the committee for the courtesy of allowing me to speak, and I will be happy to take any questions.

DR. ROBERTS: Thank you, Dr. Lamm. To point out, since you sort of just arrived today, the agency has indicated earlier that certainly their risk assessment will take cancer risks into consideration and then they plan to consult with the Office of Water in their -- as far as methodology and potency estimates and so forth for estimating those cancer risks. So it's really not among the scientific issues that are posed to the panel during this session.

But I would certainly offer panel members the opportunity to ask any questions that they might have before we move on, but would request that they keep them fairly brief.

Dr. Steinberg?

DR. STEINBERG: Dr. Lamm, as you know,

we don't have that skin cancer study. Did you circulate that study?

DR. LAMM: The one from --

DR. STEINBERG: The one that you say -- the skin cancer study that you quote from Mongolia, was that it?

DR. LAMM: From inner Mongolia. No, I did not. I would be happy to submit a copy of that.

DR. STEINBERG: And where is that in press?

DR. LAMM: At ATSDR.

DR. STEINBERG: But where is that in press? You said it's in press.

DR. LAMM: As an ATSDR report.

DR. STEINBERG: So it's a publication of ATSDR, which is not a journal, of course. That's a report to ATSDR.

DR. LAMM: Correct, but according to the NRC in their deliberations, they considered that the internal and external peer

review process of that made it equivalent for their purposes as a peer --

DR. STEINBERG: Again, we would have to see that and we would be interested in seeing that.

How many cancers -- how many skin cancers did you find?

DR. LAMM: Eight.

DR. STEINBERG: You found eight?

DR. LAMM: Yes.

DR. STEINBERG: That's a small number of skin cancers to be able to then make an assumption of threshold versus non-threshold for arsenic. And who looked at those cancers?

DR. LAMM: Those cancers were looked at by the Chinese dermatologists and confirmed by Professor Stephen Tucker, professor of dermatology at University of Texas.

DR. STEINBERG: A dermatologist. Do you have slides on those? Is it a dermatopathology? Do you -- can you tell

me --

DR. LAMM: There exists on some of them. Others are by visual determination by the U.S. professor.

DR. STEINBERG: So you don't have slides on those of dermatopathology to definitively say that those are, indeed, cancers and what type of cancers those are?

DR. LAMM: Yes, those have been reviewed. The laws of China do not allow the material to leave the country. But they have been reviewed there.

DR. STEINBERG: By dermatopathologists there?

DR. LAMM: By their dermatopathologist and by Professor Tucker.

DR. STEINBERG: So there are slides, and Professor Tucker, a dermatologist, not a dermatopathologist, has access to those slides? I mean, this is all a little -- you know, these are small numbers without really

achieving the gold standard in the United States. I think we have to be cautious about our saying that arsenic is, therefore -- that there is a threshold versus linear based on this.

DR. LAMM: Excuse me. I have not reached that conclusion. What I said is that this one study demonstrates that. And it ought to be reconfirmed.

DR. ROBERTS: This is a very important discussion, but probably not for the purposes of our panel here. I'm not trying to minimize this, but I would like to go ahead and just move through this as quickly as we can, especially since --

DR. STEINBERG: I think also related to any of the other studies in Taiwan, again, we would have to see those, we would have to know what diet they are on. I mean, these are all very complicated things and without having that information, it's very hard to comment.

I think we could leave it at that.

DR. ROBERTS: Thank you. Again, since it does not directly pertain to our discussion, unless there are some really important questions to be asked, I'd suggest that we move on.

DR. LAMM: I thank you.

DR. ROBERTS: Thank you, Dr. Lamm.

Mr. Cook, I believe we have on the schedule now a presentation by the agency on some of the exposure aspects?

MR. COOK: That's correct.

DR. ROBERTS: And let me turn it over to you to introduce that topic and the presenter.

DR. COOK: All right. I'll try to keep this brief because I know we're behind schedule.

Today, the agency would like to present to the panel a discussion of the exposure data and assumptions that we propose

to use in a children's risk assessment for CCA.

At this time, I would like to introduce the speakers at the table. To my far left is Dr. Timothy Townsend from the Department of Environmental Engineering Services, University of Florida. To Dr. Townsend's right should be Dr. Bob Benson, who is from U.S. EPA region 8.

Okay. I got it wrong. Anyway, Dr. David Stilwell from the Connecticut Ag Experiment Station, University of Connecticut. Then we have Dr. Winston Dang who will be in assistance if needed. And Ms. Doreen Aviado will make the presentation on the exposure scenario.

I would like to point out that today we have do have present -- not to put them on the spot, but we do have present exposure experts from the Health Effects Division, as well as staff from the Office of Solid Waste,

if we do reach that area, as well as staff from the CPSC if we do get into the protocols.

So I'll just conclude with that and turn it over to Doreen Aviado.

MS. AVIADO: Thank you, Norm. Good morning, Mr. Chairman, members of the panel, ladies and gentlemen. My name is Doreen Aviado. I'm a biologist with the antimicrobials division and it is my pleasure to present to you this morning an overview of OPP's proposed approach for developing the CCA child playground exposure assessment.

Based on presentations you have heard from yesterday and this morning, you are already familiar with the complexities and the issues associated with this assessment.

This morning I'll put into perspective for you the scope of the exposures and discuss in more detail our proposed approach on the methodology.

Next slide. For this assessment, it's

very important that we clarify what we intend as the scope of the playground exposures. To put this into context, we consider that residential playground settings will include schools, day care centers, municipal and public parks and home sites where CCA-treated play structures are located. The playground structures themselves would be both the treated wood playsets and any related recreational equipment and timbers that are used to border the play area for which a child may come into contact.

The playground soils would refer to any soils under or adjacent to the structures. The soils may also be considered to encompass those playground buffering materials which are found on public playgrounds under the equipment. These are used as shock-absorbing playground surfacing -- loose surfacing materials, such as the wood chips, mulch, shredded tires and pea gravel.

Specifications for these materials are set and provided by the U.S. CPSC, Consumer Product Safety Commission.

Next slide. We need to clarify also what we intend as our final approach for the exposed child, the camera snapshot, if you will, of what we're looking at for the child. We need to characterize the non-dietary exposures for a three-year-old toddler weighing 15 kilograms, representing children ages one through six wearing a short-sleeved shirt, shorts, shows, and clothing -- other clothing that certainly would be considered appropriate for warm weather conditions, while playing on playground settings. These children would be on the settings from one hour per day for 130 days per year, six years over their lifetime.

This is general schematic, just to review with you the major exposure pathways through which our representative

three-years-old would be exposed to the compounds from CCA on a playground.

In service CCA-treated wood playground structures are the source of the dislodgeable arsenic and chromium residues on wood surfaces. Also, these compounds can leach into the substrates surrounding the structures, resulting in contaminated soils and significant residues of arsenic and chromium.

The concentration of the residues, their availability for child contact via the dermal and oral ingestion routes would vary based on several factors.

For the wood surface residues, the factors are related to the nature of the wood used to fabricate these structures, the conditions on the wood surfaces, for instance, the wood type, the pressure treatment conditions, the age of the structure, the wood moisture content, if the surfaces are now

weathered or sanded, abraded or coated.

In addition, for the soil residues, factors related to exposed wood surface areas and environmental conditions apply. For example, the soil characteristics are important, precipitation patterns, soil and water pH.

Based on these exposure pathways, we propose to develop four scenarios. We've talked extensively yesterday on these, so I'll just quickly run through them.

There are four scenarios, two which are dermal: Child dermal contact with the wooden play structure; dermal with contaminated soils; child incidental oral ingestions from hand-to-mouth contact with the wood surfaces; and incidental ingestion of the contaminated soil.

For your consideration, we also have on this slide two additional scenarios that may be considered. We have spoken about

buffering materials, and there may be the possibility that we need to look more closely at developing a dermal and incidental oral ingestion scenario for the CCA-contaminated buffering materials.

One point I did want to make here is we spoke at length yesterday about wood mulch and wood chips and the propensity for a child to be in contact with those. Please consider that buffering materials also include pea gravel.

If you are not familiar with that, it's possibly a high-affinity substrate for a child. There are very small pebbles, the size of a jelly bean. And we know that children ages two, three -- our typical representative child could very much inadvertently be involved with mouthing of those types of buffering materials.

Let's move on. I would like to discuss with you now in more detail our

proposed methodology.

Our goal within OPP is to develop realistic child playground exposure scenarios. We propose to rely at this point on a deterministic approach whereby the central tendency exposure values are used to calculate the lifetime average daily dose estimates for the cancer assessment, and the high-end exposure values will be used to calculate the average daily dose estimates for our non-cancer assessment.

In contrast to methods which generate the single-point estimates of risk, which may not adequately address the uncertainties and variabilities associated with the derived estimates, we would propose for consideration an alternate approach using probabilistic techniques such as the Monte Carlo simulation.

Probabilistic techniques -- as you know, they do take into account the variability of existing data from the exposure

parameters and yield a distribution of potential exposures.

To develop realistic scenarios, we certainly need to look at the separate components. We need to select appropriate parameters to achieve this goal. These include the routes of exposure, the duration of exposure, input variables, which are subsetted as child activity assumptions and exposure factors, the residue data, concentrations on the wood, in the soil, and the equations we'll use for the dose calculations.

Regarding the selection of the residue data, I'm very pleased to have with us today sitting at our panel table Dr. Stilwell and Dr. Townsend who, as part of their discussions on the research they have conducted, they will include a discussion of the contaminated soils and surface soil residues as a comparison of the existing data sets that we're aware of

from the current data. And they will present those for the panel's consideration.

The major routes proposed for child playground exposures are dermal and oral -- and we can move to the next slide.

The inhalation exposure route at this point we have not considered. We consider it negligible.

We don't propose to do this route as a -- we don't propose to develop this route yet. It is a topic for discussion by the panel.

Our assumption today is that the exposure is negligible because of the level of surface residues not being respirable at significant concentrations. We also know that, on the wood surfaces, these are not volatile compounds.

Next slide. We spoke about this yesterday, so this will just look familiar to you. Within OPP, we have exposure durations

set from one day to one month for short-term, one to six months as intermediate-term, longer than six months, long-term, and for cancer assessment we conduct lifetime exposure durations, where the portion of the exposure is amortized over the lifetime.

For the non-cancer assessment, we proposed, therefore, for this child playground portion of our comprehensive assessment to conduct it for short-term and intermediate-term. This is based on the assumption that children are exposed for up to 130 days a year on playground structures and soils.

The cancer assessment, as we mentioned earlier, is to amortize the cancer exposure for children over a lifetime, and this is based on duration of six years out of their 75-year lifetime.

The input variables that we're considering include child activity assumptions

and exposure factors. Some of these are variables considered as general inputs for all four scenarios and others will be specific to certain scenarios.

The child activity assumptions are based on a child's behavior and anticipated activity patterns on playgrounds versus other residential sites.

This is a point of clarification, to note that when OPP finalizes the human health assessment for the re-registration of CCA, we will include a comprehensive residential exposure assessment for children in contact with CCA compounds in other residential as well as playgrounds, for instance, residential exposure to residues from decks.

OPP assumes that a three-year-old child would be engaged in sustained self-directed play behaviors on playsets and in adjacent soils and substrates. Children at this age are assumed to be capable of play

activities that are independent of a parent or guardian.

Also, we assume that children at this age will exhibit frequent hand-to-mouth behavior and soil mouthing behavior.

The exposure factors are measured inputs and they are not necessarily based on a child's activity patterns. These are agency default assumptions from peer-reviewed data sources. This slide shows you the sources of our inputs.

The guidance document shown here -- there are three listed -- they are relied upon for conducting agency exposure and risk assessments, and they may be familiar to most of the panel members.

The California Department of Health Services study of 1987 presents an analysis of CCA residue data collected from numerous field tests on wood structures in outdoor sites across that state, including parks and

playgrounds, and it's cited here because the study provided useful information on estimating the frequency of child playground visits.

The following slides will identify the data we propose to use for each of our input variables. Each slide shows you the source of the input and whether they are central tendency or high-end values.

We'll cover the child activity assumptions first.

For the exposure frequency, we're proposing 130 days a year on playgrounds. This, as you see, is based on the California work. It assumes five times a week, 26 weeks a year. OPP considers this a central tendency value. However, in the California study, it was used to estimate high-end exposures.

This is an important input because, as you have heard from some of the public comments, we may be tending to underestimate

what would be expected as child play behavior in southern, warm weather geographic regions.

For exposure duration, we are proposing to use six years for a child engaged in outdoor play activity on residential sites. This is adopted from Superfund's draft guidance, and the value is not necessarily specific to playground sites, but was selected by OPP for this assessment based on professional judgment.

For the exposure time, we propose values of one hour a day and three hours a day as the time a child will spend engaged in outdoor play activity. They are based on data of high confidence for school grounds and playgrounds. Note that these values are proposed for developing the dose estimates in the oral ingestion scenario involving hand-to-mouth contact with the wood residues.

The one-hour-a-day value as a central tendency input will be used in conjunction

with a hand-to-mouth frequency of 9.5 events per hour, and the high-end value of three hours correlates to the 20 events per hour hand-to-mouth frequency.

The proposed soil ingestion rate values are 100 milligrams and 400 milligrams, and these are based on data of medium to low confidence due to limitations in the studies from which the values were derived.

The proposed hand-to-mouth frequency of 9.5 events per hour and 20 events are based on data generated from videotaped observations of children in home and day care environments, and the frequencies were, in fact, recommended by the SAP in their 1999 meeting with the agency for adoption into the latest version of the residential SAPs.

For the exposure factors, the data input shown here for age, body weight and life expectancy are considered standard agency inputs and they are derived from data we feel

are of high confidence.

The proposed body surface area of 1640 square centimeters for dermal contact surfaces of exposed hands, arms and legs -- it's based on data for soil contact clothing scenarios for children wearing short-sleeved shirts, shorts and shows.

This value depicts 25 percent of a three-year-old's total body surface area at the 90th percentile, and it takes into account that, even with clothing, the portions of the skin under the clothing may be potentially exposed.

The hand surface area measurement of 20 square centimeters was selected as a more realistic estimate by the agency for this assessment as opposed to the assumption of children using whole hand surfaces. The 20 square centimeters is recommended for screening level estimates, again, by the SAP in their 1999 recommendation to the EPA.

For fraction ingested, we propose a 50 percent removal efficiency of residues from fingers by human saliva based on studies for organic chemical pesticides.

Without data specific for transfer of residues from playground soils to hands, we relied as a surrogate on an assumption of a one-to-one relationship of dislodgeable residue transfer based on transfer dynamics for turf to skin.

We propose to use an adherence factor of 1.45 milligrams per square centimeter to best represent the playground soil substrates. Existing data recommendations in our exposure factors handbook for soil adherence to skin are rated of low confidence due to associated data limitations and high variability.

So what we did is we took a look at guidance offered by EPA Superfund program. We adopted their 1.45 value based on their commercial potting soil data from the

Superfund risk assessment guidance document of 1989.

They have updated their guidance. There is a current draft Superfund guidance document issued in 2000 which offers additional data for adherence factors based on results from studies conducted with children with dry and wet soils, indoor/outdoor settings. And OPP will need to determine the suitability of these data over our proposed value for use in this assessment.

Now, I have a few tables here. The benefit of the table would be just to point out for the panel which values we would like you to focus on.

These next slides here are tables which overview OPP's ranking of the proposed input variables for use in calculating the exposure estimates. I want to qualify -- the column that says OPP data confidence specifically is our confidence in proposing

the value for the assessment as opposed to the confidence of the data point itself within the study which we're citing.

OPP's level of confidence is characterized as low, medium or high. The tables are intended to help the panel focus discussions on the variables of low to moderate confidence which we highlight here as either general or scenario-specific factors.

For example, the proposed exposure frequency and duration may truly underestimate exposures for children spending considerable time in the warm-weather geographic regions.

Our overriding concern in conducting this assessment is to make sure that the over or underestimation of exposures are somehow minimized.

We can scroll through the rest of these just to give the panel a look at these.

Now, the last set of slides we'll look at will be for the equations for the exposure

dose.

These equations are derived from standard exposure algorithms found in our EPA residential SOPs. The non-cancer dermal and oral ingestion doses are derived from the average daily dose equations yielding maximum estimates of short and intermediate-term exposure.

Our cancer dermal, oral ingestion doses are derived from the lifetime average daily dose equations to yield central tendency estimates representative of exposures amortized over a lifetime.

The non-cancer ADD equations are shown by scenario as follows: This first slide is for dermal contact with wood.

I would like you to just note here that we propose to use the maximum arsenic and chromium residue concentrations from the wood surface residue data and apply a dermal absorption factor as proposed in yesterday's

hazard characterization presentation, 6.4 percent for arsenic and 1.3 percent for chromium to account for the oral toxicity endpoints in this dermal scenario.

For the dermal contact with soil, note that the equation is expanded here to include an adherence factor, and that we propose to use, again, maximum levels for soil residue concentration data.

For the hand-to-mouth oral ingestion of wood residue scenario, aside from the inputs that have already been noted, we plan to use high input values, as you see here, for the frequency of hand to mouth, the exposure time, and apply a fraction ingestion.

For the oral ingestion of contaminated soil, we include the maximum reside data and high-end inputs for the soil ingestion rate. And we are applying here, as you see, based, again, on the hazard characterization -- we're proposing the 25 percent bioavailability

factor be applied for the arsenic from the soil ingestion.

The cancer LADD equation for both dermal and oral ingestion, they include the ADDs, which are derived using the average values, and the central tendency inputs for one hour for the exposure time, 9.5 events per hour for the hand-to-mouth frequency, and the soil ingestion rate of 100 milligrams per day.

That concludes my presentation for this morning. Thank you for your attention. I'll be happy to take any questions you may have at this time.

DR. ROBERTS: Thank you, Ms. Aviado. Do I have a -- holding comments, of course, until later, are there questions among panel members?

Dr. Morry and then Dr. Clewell.

DR. MORRY: With regard to the soil adherence factor and so forth, do you have any data on what kind of soil is actually

underneath these play structures, like what percentage of them have wood chips, what percentage have sand and so forth?

MS. AVIADO: What I'll do, Dr. Morry, is try to clarify the issue, and if someone else here from the agency has additional information, I will certainly hand the mic over to them.

What I want to clarify for you, because the playground setting, the residential setting includes both public playgrounds for which CPSC specifies these buffering materials, and homeowner backyard playsets for which there are no specifications, you have a wide range. You have soils -- depending on the soil characteristics of the geographic area, you have wide variability just in the true raw soil under a playset.

There are protective substrates, as we mentioned, these buffering materials, which

you would be more likely to find in public playgrounds. There are statistics that show that, even though there are specifications for what we would like as surfacing, whether they are adopted or not, the enforcement of that, there may not be 100 percent enforcement. There was a survey that showed between 70 and 90 percent of the public municipal playgrounds do have buffering surfaces.

DR. ROBERTS: Dr. Clewell?

DR. CLEWELL: You will have to remind me what CF is in the non-cancer equations. It's not mentioned on the slides.

MS. AVIADO: The nature of our non-cancer equations?

DR. CLEWELL: No. CF. There is a term "CF" in the non-cancer --

MS. AVIADO: Oh, I'm sorry. Conversion factor. That's just a simple conversion factor --

DR. CLEWELL: That would be -- oh,

units?

MS. AVIADO: -- from units to --

DR. ROBERTS: Dr. Wargo and then Dr. Thrall.

DR. WARGO: Thank you. That was an excellent presentation. A few quick questions.

I'm interested in your judgment about data confidence. And you have applied this judgment across a variety of the factors that you are considering.

Could you give us some indication of how you might classify a factor as high confidence versus moderate or low confidence.

MS. AVIADO: I would be very happy to do that for you, and I'm glad you brought that issue up because I think this will be central to our discussions tomorrow.

DR. WARGO: Excuse me. And before you do that, what I'm interested to know is what the rating of confidence would do to your

judgment about the selection of the magnitude of the factor that you choose or the range.

MS. AVIADO: I will do the best I can to at least address a portion of that. Your second part of the question is much more involved. I will certainly defer to others from our agency to help me answer that, or they can address that issue.

But in basic terms, the tables were meant to show you our confidence in applying the input for the exposure estimates for the playground settings.

The first table showed age, body weight and life expectancy as high confidence for us because those are considered standard defaults. We don't assume that those would be debatable inputs.

The exposure frequency was moderate to low confidence because, even as you've heard in the public presenters, there is much concern that we are underestimating child

activity, child frequency of visits on playgrounds.

I would say there is an element of professional judgment and subjective decisionmaking that went into preparing the table. They are based on our stance as we sit here with you today.

There was not a true methodology to validate our selections. That's why we would like more input from the panel.

But let me just continue to assist you. The six-year duration is noted here as moderate because it may or may not represent the length of time that children do spend on playgrounds, especially if you are considering home playgrounds where they may spend more time. There may be children spending less time than six years, so it's moderate confidence. There is a lot of variability we anticipate.

The body surface area measurement we

have high confidence in because it was based on the 25 percent of the 90th percentile body weights that are averaged in the child-specific exposure factor handbook. The male/female body weight totals are averaged, and that 25 percent is documented specific as appropriate for clothing scenarios in warm weather settings, children with short-sleeve shirts on, shoes and shorts. And it seemed appropriate to us that that would transition very well into a playground assessment.

For moderate confidence -- we rated the 20 square centimeter hand-to-mouth surface area of the three fingers moderate because there is not enough site-specific data conducted to observe children on playground settings for us to know 100 percent if three fingers is appropriate. They may be putting more hand --

DR. WARGO: I appreciate you going through each of these, but my question was

more generic.

As your perception of the uncertainty surrounding our understanding of each factor increases, so the more uncertain the understanding is, would that cause you to choose a higher bound, more conservative default assumption?

MS. AVIADO: If we were sticking with a deterministic point estimate approach, we probably would certainly want to look at the high end because of the level of uncertainty within each of the parameters.

It may, in fact, give us the springboard to consider truly maybe as a screening tool, the deterministic point risk estimates, and then, from there, really conduct more of a Monte Carlo type simulation or probabilistic simulation because of the nature of the variability within the inputs.

DR. WARGO: One very minor question.

Do you consider the variability in

exposure that might occur from the result of thumb-sucking behavior as the dad of a couple of former thumb-suckers?

MS. AVIADO: As you see, we haven't separated it out as significant. And, in fact, initially when we were scoping out questions for the panel, one of our thoughts was because the developmental differences of children from 18 months to two years, let's say, as a snapshot -- their behaviors may be distinct from children who are already three and include higher frequencies, as Dr. Freeman is nodding there to acknowledge.

We were considering whether we should even, in terms of the surface area body weight parameter, consider a ratio that might be more reflective of that. But as a subset of this population, we have not considered just the thumb-suckers.

And I would just want to -- before I forget, I wanted to make a quick point that,

other than those buffering scenarios, it would be worthwhile for the panel to help us work through any additional scenarios that would be appropriate to characterize the exposure.

We heard yesterday the importance of considering maybe splinters that children would have as occurring to them on playgrounds. Also, we heard abraded skin in contact with the wood. And these sorts of things we would appreciate consideration of.

DR. WARGO: One final thought. The window of exposure you are measuring the variables of behavior is six years. I'm assuming that you are choosing that because you believe that variability in behavior and variability of exposure that would occur within that six-year window is irrelevant to the judgment about the risks that the children develop.

MS. AVIADO: Initially, when this was scoped out for a preliminary assessment, that

refinement was not taken into consideration.

DR. WARGO: So that the exposure at year two, you are saying is equivalent to the exposure at year six?

MS. AVIADO: Correct. If you look at the approach as presented, correct. That three-year-old, as representative of all behaviors, all potential exposure scenarios for children one through six. Correct.

DR. WARGO: Thank you.

DR. ROBERTS: Dr. Thrall?

DR. THRALL: This is probably a naive question because I'm coming from completely outside of this area, so bear with me.

But we've spent a day and a half talking about lots of really very variable things, many of which are very subjective: Type of wood, type of soil, amount of dislodgeable arsenic, time on playground, amount of hand-to-mouth contact, number of fingers put in mouth, whether they're

thumb-suckers and so on and so on. So my question is, why don't we just take a large number of children and measure the amount of arsenic that's in their urine and then just absolutely know what their risk is?

Is it detectable at these levels?

MS. AVIADO: I would like to defer that question for you. I'm going to defer to Dr. Winston Dang sitting next to me.

DR. DANG: My name is Winston Dang. Your question is very interesting and, actually, we discussed it with Dr. Andrew Smith a few months ago and we are very interested to understand his research.

As a matter of fact, if we have a large data of biomonitoring studies, that data would be very helpful to us. We can determine how is the real world, realistic estimate of the number we can get from the exposure.

And biomonitoring either from urine or from hairs.

So, again -- one of the panel may give a better answer than me in this question here.

DR. ROBERTS: I'll follow up and then I have a number of other people that want to raise questions as well.

DR. CLEWELL: I just wanted to point out that they primary source of arsenic is in the food, and that secondary would be water, and that we all have significant levels of arsenic in our urine and, yes, it's measurable.

The question is whether the contribution from playground equipment contact could actually impact the levels in the urine compared to the much larger, at least order of magnitude, even by the most conservative estimates, contribution from the food.

And if you look at the gradient document, which is about an inch and a half thick -- but in the middle there is a summary of the epidemiological studies conducted on

people who work with CCA-treated wood. So these are workers exposed to the wood in a much more intimate fashion than the children. And some of the studies show increased urine levels and some do not. So even in that case, they weren't able, in some cases, to detect an increased urinary level of arsenic.

DR. ROBERTS: I'm sure this topic will come up when we get into our issues in terms of possible approaches.

I had Dr. Ginsberg next, then Dr. Styblo, then Dr. Smith.

DR. GINSBERG: Regarding the use of the three-year-old as a surrogate for the one to six-year period, that wouldn't concern me too much if it was just an LADD you were calculating, but it sounds like you are also gunning for a one-year or a very short-term acute exposure. So I was wondering if you thought about how those acute exposures would be calculated and whether the three-year-old

is reasonably conservative for an acute exposure for, say, a younger child? And I have a couple other questions. I just want to hear the response to that.

MS. AVIADO: That's a very good point. Thank you for raising it. I think that really does illustrate the complexity of doing an assessment like this. Because the exposures can be from one day to 130 days, it may make sense to choose a more sensitive subpopulation for those acute exposures.

Did we consider that before we came to you? I would say no. We were looking in more broad terms in this preliminary approach, and we were certainly wanting to refine it through your input. And that's a very good suggestion.

DR. GINSBERG: As a follow-up, the hand-to-mouth videotapes, was that -- the essential tendency and the upper bound that you are using, is that for a three-year-old

child? And is there a distribution of data for various ages?

MS. AVIADO: I'll start off on the response on this, and I may ask for Dr. Dang's assistance.

Those are videotaped behaviors observed for children within an age range that would include three year olds. These are day care settings. They were monitored over the course of a 24-hour period, both indoor and outdoor.

So part of our uncertainty with that, even though the data itself is high confidence, is how appropriate those indoor dust sort of -- you know, you are extrapolating your thinking in terms of the wood surface dust into the mouth. How realistic those events represent child exposed to outdoor wood surfaces as opposed to indoor day care, you know, mouthing behavior? I mean, there may be some refinement required.

We have -- we are so pleased to have on the panel Dr. Natalie Freeman who certainly was intimately involved in the generation of that data with some of the Dr. Reid, Dr. Freeman studies we've relied upon to make these estimates.

I'm not sure if she would like to further clarify the nature of the subsets within that study because it was quite involved.

DR. FREEMAN: The Reid videotaped data, which is based on 30 children, 10 of them were in homes and the other 20 percent were in one day care program. The ages of the children ranged from -- I believe it was about not quite two years old to five years old. And, on average, they were three-year-old kids.

The hand-to-mouth data -- I should say that for most of the kids, we were observing them for seven to eight hours a day so that --

and within child and also between child, there is an enormous amount of variability in these behaviors over time.

The 9.5 -- we have since been looking at another 60 kids on the border of Mexico and Texas on the Texas side, ranging from 6 months to 48 months old. And we find that for the three to four year olds, the 9.5 shows up again, and that is substantially less than the 6-month-old to 18-month-old children, where there is a great deal more mouthing.

One of the things I guess I was going to bring up tomorrow but I might as well say it since I'm talking, is that the 9.5 is based on the eight hours of observations. This includes both indoor and outdoor environments.

What we see when children are actively playing outdoors, that for the most part, other than little kids, the under 18 month olds, is that mouthing outdoors is less frequent -- and we'll be able to provide you

with some of this data broken down by indoor and outdoor, which I think you might be able to use.

That most of this is during down time. It's during quite time. They have come indoors. They are watching television or, if they are in the day care program, they are listening to story time. And that's when the mouthing becomes very, very active.

It doesn't necessarily mean that they aren't consuming things that they acquired outdoors, but it's not in that outdoor location.

MS. AVIADO: Thank you for qualifying that for us.

DR. GINSBERG: And I just had one more quick question. Your relative bioavailability factor for soil ingestion of 25 percent, that's just for soil ingestion? The dislodgeable ingestion, that doesn't apply to? Is that correct?

MS. AVIADO: That is correct. It is just for the one scenario of the arsenic for the ingestion from soil. The others are assumed 100 percent.

DR. ROBERTS: Next on the list I have Dr. Styblo followed by Dr. Smith, Solo-Gabriele, Mushak and Kosnett.

DR. STYBLO: I will ask my questions later. I'm fine.

DR. ROBERTS: Dr. Smith?

DR. SMITH: Your equation for doing the ingestion scenario for hand-to-mouth contact, as I understand it, this is the concentration -- or this is the data from the wipe test; is that correct? So this is going to be micrograms per centimeter squared.

MS. AVIADO: Correct. This would be the wood surface dislodgeable --

DR. SMITH: Wood surface dislodgeable estimate.

And then you apply that to a surface

area of a hand, assuming a one-to-one relationship. Is that correct?

MS. AVIADO: Correct.

DR. SMITH: So just help me out. I just want to make sure I understand the logic of this.

We have some -- wipe method, be it a block or a cloth, we wipe some 100 centimeters squared, so there is some accumulation onto the surface, and we get some number. We normalize it over 100 centimeter squared.

You assume that when you put the hand down on the surface, that there can be no accumulation on the hand, that all you can get is the same concentration. Is that correct? So on the empirical data, you are allowing for accumulation, but are you not allowing for accumulation on the hand. Is that correct?

MS. AVIADO: I don't believe it's correct to view it that way. I would like more clarification for you, Dr. Smith. I'll

have Dr. Dang walk you through that scenario.

DR. SMITH: Thank you.

DR. DANG: We understand they have some uncertainty associated with this. Yesterday, we have a lot of presentations between wipe test and also the hand press. And those tests, some are very variable, is from 25 percent, and some is -- like 1987, CDHSS have some studies show between those two tests, it's 100 percent.

But uncertainty associated with this is, so far, we have a very limited data to show the true values of that residue on the surface of the wood.

So in other words, those transfer residues -- in here, we have to assume it's 100 percent. Those residue transferred to the wipe, test, 100 percent transfer to skin.

But here we say we don't have real data to see here is because all the data we show here we understand that transfer

efficiency is highly dependent on the moisture of the content of the hands and also some texture of the skin and also is wood type and age of the types.

So that is a lot of uncertainty where we associate with this kind of transfer efficiency.

But here in our equation we had to use the best available and best estimate we have from available data in the last 25 years. We can select the best credible studies we can have to use into the equation.

DR. SMITH: Let me rephrase the question because I think we'll get into extended discussion on this during the questioning period.

With the existing data sets, and there are a few out there that have both hand and wipe test data, in some cases for other pesticides, in some cases for CCA wood, have you attempted to use that data to validate

your assumption of this equation model?

MS. AVIADO: Can you further elaborate what you mean by validate?

DR. SMITH: There are some data sets where you could actually start with a microgram per centimeter squared from the wipe test data.

And then there is calculate based on your model what you would expect for loading on the hand and compare it to the observed loading on hand to see if your model holds up to a test.

MS. AVIADO: As you can appreciate, we have only developed thus far a very preliminary approach, deterministic. We haven't used models to help us simulate.

DR. SMITH: This is just a question of using the empirical data available. Running a calculation from two sets of the data and seeing if they compare well.

There is a gentleman with his hand

raised in the back.

MR. MOSTAGHIMI: My name is Siroos Mostaghimi, and I work with colleagues in antimicrobials division.

I think you have a good point. We basically got to that point, that we have all of our empirical formulas and everything and we were starting to try to do that. This is the process we're going to go through if we cannot find more reliable data. Whatever we have, we're going to look at it.

One way we were thinking was that one. It's a very good suggestion. The problem we had so far is that there is so much variability among the data that you really don't know which one is the best one. That is one of the things that we're asking the panel to make to comments on, reliability of data, and afterwards we'll take care of it.

DR. SMITH: One last question again regarding to the validation of the model.

Have you looked to see if there are any studies out there which determine whether or not implicit assumption of linearity in the transfer efficiency. In effect, you go out and somebody wipes 100 centimeters squared, they get a certain mass, they normalize it to 100 centimeters squared and they say now we have so much micrograms per centimeters squared. So they basically assume linearity.

Have you looked to see if there are any studies that would tell us if we happened to do those experiments, but instead of wiping 100 centimeters squared, wipe 200 centimeters squared or 400 centimeters squared or 10 centimeters squared would we get the same transfer efficiency.

I'm asking the question in somewhat -- because I think the question is no, there is no data for that.

MS. AVIADO: That is the answer at this point. We have not done that level of

analysis. We'll be hearing in some of the later presentations a little bit more about the existing data sets and some of the variability. So maybe those issues can be discussed then.

DR. ROBERTS: Dr. Solo-Gabriele?

DR. SOLO-GABRIELE: I was interested in getting some more information concerning the exposure frequency and exposure duration, the 130 days per year and the six year time.

Were those taken from the U.S. EPA Exposure Factor Handbook? And, if so, how did those numbers -- how were those numbers derived for that handbook?

MS. AVIADO: I'll address that. The 130-day frequency, because the Exposure Factor Handbook does show some daily calculations for the amount of time in minutes per day that children spend on playgrounds or outdoor on school yards, the factors handbook does not characterize how many days per year a child

visits playgrounds, what we ended up doing is we took a look in more depth at some of the assumptions made by the California Department of Health Services Study and from professional judgment went ahead and determined that that 130-day frequency may be adequate as a central tendency.

In terms of the basis for their assumption, they ran through some exposure calculations, assuming the child would have low moderate and high exposures. For their moderate exposure frequency, it was closer to 78 days a year, their high-end was five days, 26 weeks out of a year -- five days a week, 130 days at their high-end.

But the actual basis for that number, I think from our viewpoint, we chose it as a possible appropriate input from professional judgment.

Your other question, I believe, was the six year.

The six year we adopted using Superfund's approach. They have an age adjusted factor approach to when they do exposure risk assessments where they will break out certain subpopulations for certain exposure scenarios.

And, again, our own exposure factor handbook, which we tend to rely quite heavily on, did not cover what we felt might be the appropriate exposure duration information for this scenario.

So for lack of really adequate data, site-specific data for playgrounds, we made the assumption again that maybe the Superfund guidance would be more appropriate, and we based it on that.

DR. DANG: I believe Doreen just mentioned about the Superfund six years old is for residential sites. It is not necessary for playground equipment. She mentioned in her presentation already.

DR. SOLO-GABRIELE: I agree with earlier comments that were made that it may underestimate especially in the southern climates, both the frequency and duration.

MS. AVIADO: Right.

DR. ROBERTS: Dr. Mushak.

DR. MUSHAK: Let me change the focus of this and ask some clarifications about jurisdictional issues between offices, because you are constrained, as I understand it, to those exposure scenarios that entail end use aspects of treated wood, right?

That is, you will never meander off the reservation of OPP requirements as to what you can do and not do.

To the extent that there are other exposure scenarios out there that are further downstream, say, with disposal and recycling, do the solid waste folks, if they are here, have some role in collaborating with you folks?

The second question related to that is what happens with this stuff in terms of what are the levels of hazards that may be raised?

I realize that this is not regulated as hazardous waste provide you leave it intact. But any recycling scenario that I see that would be feasible without filling up landfills requires doing something with this.

It seems like that generates hazardous waste. How does OSWER deal with that?

MR. COOK: Let me make a few comments. Then I'll ask my OSWER colleagues to step up to the microphone.

In the life cycle of the process, you have the manufacturer of the pesticide, and usually OSHA handles the workplace issues. Then you get into the wood treatment. We would actually do the risk assessment for the workers.

But any of the emissions, you have the Clean Air Act, you have the Clean Water Act

and then you have RCRA that get involved. Then when you get into the actual end use, that's primarily the big area where FIFRA comes into play.

As Debbie mentioned earlier, most of the thrust of FIFRA is at the pesticide. Actually, the wood is a treated article. But because of the unique risk characteristics, obviously, we're looking at the risk of treated wood. Then when you get into the disposal area, that's where OSWER comes into play. I will defer to them. I don't know if they want to make a few comments. We do have two representatives here.

MR. ELLIOTT: Ross Elliott. I'm not really sure what your question was about the interaction between solid waste and pesticides? What --

DR. MUSHAK: Will there be an interaction. And second, can you take us through the sequence of regulating the

disposal aspect of the lifetime of treated wood.

I know that there is this issue of you don't particularly treat it as a hazard.

But if you try burning it, then that gets you into the Clean Air Act. If you try burying chips, that becomes a hazardous waste, presumably. What are the options for disposal that trigger different regulatory --

DR. ROBERTS: Let me interject. Is this -- I want to understand how this question is going to pertain to sort of the issue.

DR. MUSHAK: It's trying to get a feel for all of the exposure scenarios versus those that are resident in our charge.

I'm perfectly happy to let it go. It seems like we're looking at a very narrow picture.

DR. ROBERTS: Let me suggest this. Perhaps you guys could talk sort of off-line at lunch. And if it looks like there is an

issue that pertains to feedback that we might want to provide in terms of exposure assumptions or scenarios, then I would encourage you to bring that back in when we have that discussion.

DR. ROBERTS: Dr. Bates?

DR. BATES: I want to go back to the issue of hand-to-mouth oral ingestion of residues.

There is a factor in here for hand-to-mouth frequency of 20 events per hour and a fraction ingested of 50 percent.

This seems to imply that there is a sort of reloading every three minutes of the hand. It seems to me that might be a little unrealistic.

I was wondering if any consideration might be given to another factor in here like a reloading frequency or something of that nature.

MS. AVIADO: That's a very good point.

I think it was illustrated actually this morning when Exponent showed some of the pie charts to show the large numbers attributed based on this high frequency of hand-to-mouth.

At this point, we are certainly open and encourage discussion from the panel to help us work through a much more realistic scenario.

That additional consideration for a different component into the equation we have not presented that, but we certainly would want to consider it.

The idea initially was that because it is a one-to-one transfer, that 50 percent based on the efficiency from saliva reduces that load. But you are correct. In our assumptions, we are assuming that the same amount of surface residue is constantly reloaded onto those three fingers into the mouth.

In terms of working through a more

realistic equation that would be encouraged for the panel to help us work through if you do have some suggestions.

DR. ROBERTS: Dr. MacDonald and Dr. Ginsberg.

DR. MacDONALD: Given the difference between wet and dry hand uptake, I'm surprised the model is not including time with wet weather play.

And my other question is there doesn't seem to be a simple relationship between exposed dermal surface, the contact surface and the arsenic loading. In fact, the limited data we saw on the SCS study suggests even a zero or negative correlation between hand size and loading.

It would seem to me that these factors would make a model like you are proposing very tenuous.

DR. ROBERTS: Dr. Ginsberg?

DR. GINSBERG: Regarding the

California use of the 130 days a year as an upper end exposure, I just wanted to add to your consideration that they were dealing with play structures that were not in people's backyards.

This wasn't residential. So a child would have to travel to a school or municipal playground. So I think that's why they may have had a different exposure frequency mindset than what we might be thinking of in terms of this panel.

MS. AVIADO: That's a very good point. That's why we appreciated, in addition, the public comments from the gentleman from South Carolina and Ms. Applegate yesterday to really encourage us to look at more realistic --

DR. GINSBERG: I know we'll be spending time later talking about how we're going to make recommendations on dislodgeable data sets and soil data sets for you to plug into these equations. But you have also, EPA,

has reviewed these data.

And what was your thinking in terms of how you were going to select a C-max for soil and a C-average for soil and a C-max for dislodgeable?

MS. AVIADO: As Dr. Mostaghimi relayed to the panel when he gave us some input as to the current status of the agency's evaluation, we are just beginning to take those data sets, try to take a hard look, number one, at is this treated wood from a wood treatment plant or in-service playground structure?

There are certain parameters or criteria that we're sorting through to try to make better sense of this large set. In fact, the soil residue data seems to be much more of a smaller concise data set when you compare it to all of the numerous studies done on dislodgeable residues from wood.

We try to look at the methodology. We try to look at the conditions for which the

wood may be weathered or if the protocol took into consideration any sort of simulation of real use conditions for the wood. There are so many variables.

In fact, as I mentioned, we're just starting to look at this. But that would be our natural progression, to take dry wipe studies, hand wipe studies, kim (ph) wipe studies, vacuum brush studies. Try to compile them into subsets, then really analyze them for applicability to this scenario. And we have just begun to do that.

DR. GINSBERG: One final clarification. Where did the 50 percent factor come from in terms of how much will get off the hand and into the mouth.

MS. AVIADO: Actually, that is based on data from the residential SOPs and the Exposure Factor Handbook as based on data for children in contact with organic pesticides.

Clorpirophase (ph) and some of the

organophosphate. So it is measured data.

DR. DANG: We probably have to conduct uncertainty analysis and maybe if we don't have enough database, we probably have to look into the sensitivity analysis.

Because those database, whether we're going to use C-max, maybe have impact for the risk.

So we have to be conduct more further studies on those huge dislodgeable data set and also soil data set also.

And regarding those 50 percent removal efficiency, what we are concerned is we understand there is maybe a lot of uncertainty associated with this 50 percent. Because so far that is variable data from 1994 to 1998. We look at those data. Most spike test due to spike test on the test tube, either on test tube or furniture or toys.

We don't have any spike test from any wood. So we don't know that from wood to the

skin and from skin to the mouth.

We just mention about best test. The published article mostly is from organic chemical. We have to consider lipophilic and hydrophilic issue of the inorganic matters here.

DR. ROBERTS: Let's take one more short question from Dr. Smith.

DR. SMITH: Thank you, Dr. Roberts.

A question on your policy on probabilistic analyses.

Through your presentations I have seen over the past couple days the key word I always see next to any sort of mention of probabilistic analyses by the agency is the word variability.

What is the agency's policy on undertaking probabilistic analyses to get at an issue of uncertainty. I think we can all appreciate here we have got not only a question of variability, but we have

considerable questions of uncertainty as well.

DR. DANG: So far we use a so-called point estimate technique. We're looking where we can use so-called distribution estimate and use probabilistic base model.

We are shopping around what kind of model is the best for this CCA case studies.

Fortunately, we have our sister office in ORD. They currently develop a model called SHEDS model, Statistic Human Exposure Data Simulation model.

They use two-stage Monte Carlo approach to get rid of this. And hopefully we can have a more detail on this model we can use it to consider for those model perimeter (ph) and model pass away exposure analysis.

DR. SMITH: Just to clarify. By two stage, you are referring to the two stage uncertainty versus variability approach is that it's sometimes used in probabilistic analyses to get at both? Is that correct?

DR. DANG: That's correct. The amount as far as I know is include of the variability analysis also, uncertain analysis also.

DR. SMITH: Thank you.

DR. ROBERTS: Thank you. The next item up is a presentation by Dr. Styblo.

How about if we start after breaking for lunch with yours? I think the panel could probably use a little nourishment. I'll ask them to eat something light so they will be alert for your presentation.

Let's convene -- it is 12:45 now. Let's convene in one hour, promptly. Be ready to start.

(Thereupoun, Volume I of II concluded.)

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I, Frances M. Freeman, Stenotype Reporter, do hereby certify that the foregoing proceedings were reported by me in stenotypy, transcribed under my direction and are a verbatim record of the proceedings had.

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